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# BRAIN

## A JOURNAL OF NEUROLOGY

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# Brain

## A Journal of Neurology

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MARCH, 1933.

BRAIN.

PART 1, VOL. 56.

# THE DERMATOMES IN MAN,[1]

BY PROFESSOR O. FOERSTER,
*Breslau.*

THE nervous system preserves more than any other part of the human body the original division of the embryonic tube into metameres. The spinal cord is divided in segments, each segment being provided with a pair of anterior and posterior roots. The area of skin which is supplied by the fibres of a certain spinal root is called a *dermatome.*

The skin is innervated by the posterior roots as well as by the anterior. The former carry the afferent sensory fibres and efferent fibres subserving vasodilatation. The anterior roots carry efferent motor, sudorific, pilomotor and vasoconstrictor fibres, and also afferent sensory fibres. In this lecture I shall deal exclusively with the fibres passing by the posterior roots.

There exist two different methods for the determination of the area of skin subserved by a certain posterior spinal root, the *anatomical method* and the *physiological method.*

The anatomical method, used first by Herringham and later chiefly by Bolk, consists in following up the fibres of one single root by anatomical dissection through the plexus and the peripheral nerves into the skin. Fig. 1 shows the second, third and fourth cervical dermatomes as outlined by Bolk by this method, and fig. 2 the areas of the roots supplying the arm, that is the fifth, sixth, seventh and eighth cervical and the first and second thoracic roots. Each of these dermatomes occupies a different area and these show very little or no overlap.

It is obvious that this method, used by Bolk, has the disadvantage that by anatomical dissection it is impossible to follow the terminal and finest ramifications of the sensory nerves in the skin. The areas outlined by it certainly show the shape and the position of the dermatomes, but not their full extent.

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[1] The substance of this article was included in the Schorstein Lecture delivered at the London Hospital, on October 18, 1932.

To Sir Charles Sherrington we owe our knowledge of the complete topography of the dermatomes in the monkey. The method used by him, and called the method of " remaining sensibility " or the " isolation method," consists in dividing a series of contiguous roots above and below a single root which is preserved. The area of the skin, the sensibility of which is preserved after this procedure, represents the sensory dermatome of the intact root.

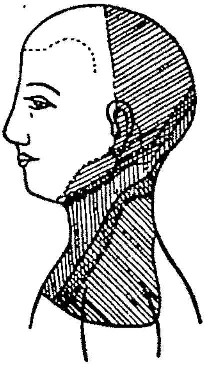


FIG. 1.

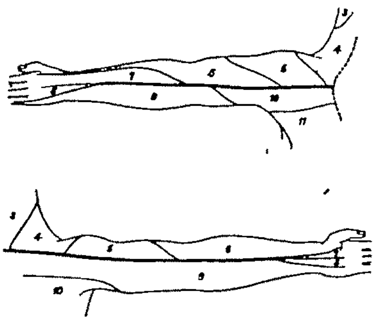


FIG. 2.

FIG. 1.—The 1st, 2nd and 3rd cervical dermatomes, according to Bolk.

FIG. 2.—Dermatomes of the upper extremity; the 4th to 8th cervical, and 1st and 2nd thoracic (9 and 10), according to Bolk.

Fig 3 demonstrates the second, third and fourth cervical dermatomes of the monkey; these overlap to such a degree that the area of the third cervical root is supplied to its full extent by the second and the fourth cervical roots.

A similar condition exists in the upper extremity (fig. 4). The fifth cervical dermatome, for instance, overlaps with the third and fourth on the one hand and with the sixth and the seventh on the other. The amount of the overlap of the different dermatomes is so considerable that division of a single root produces no loss of sensibility.

Another physiological method for the definition of the dermatomes is based upon local strychnine intoxication of the posterior roots. After segmental application of strychnine to the dorsal surface of the cord a sharply circumscribed skin field becomes hyperæsthesic, as Dusser de

Barenne has demonstrated. The hyperæsthetic area is identical in shape, situation and extent with the dermatomes defined by the isolation method, and the same large degree of overlap of adjacent dermatomes is apparent.

Our knowledge of the dermatomes in man is chiefly based upon the work of Sir Henry Head, who collected a large number of cases of herpetic eruption. Herpes is supposed to be an inflammatory lesion of the spinal ganglia, producing an eruption upon the skin in the corresponding cutaneous area. Head also contributed valuable information on the dermatomes in man by outlining carefully the borders of the hyperæsthetic skin areas in visceral disease, and the distribution of anæsthesia in traumatic lesions of the cord and the cauda equina. In Head's scheme (fig. 5) the cutaneous root areas overlap very little, and in this respect it does not conform to the results of experimental physiology. How is this discrepancy to be explained? Do monkeys and men differ really from each other so much in regard to such a fundamental organization as metamery?

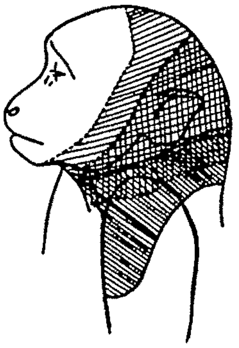


FIG. 3.

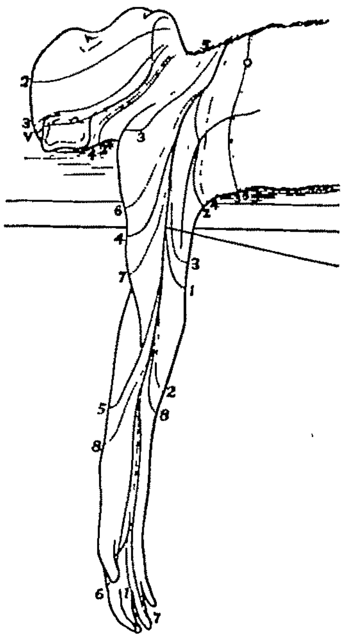
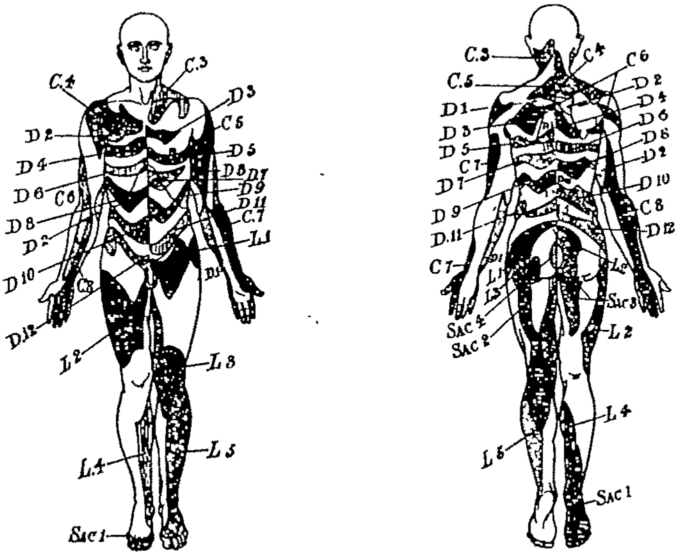


FIG. 4.

FIG. 3.—The 1st, 2nd and 3rd cervical dermatomes of the monkey, according to Sherrington.

FIG. 4.—Dermatomes of the upper extremity of the monkey, according to Sherrington.

I have had the opportunity of defining a great number of dermatomes in man by exactly the same method as that used by Sherrington, that is by outlining the borders of the sensibility which remains after a large number of contiguous roots have been divided, and a single root in the middle of them has been left intact. I need not discuss here the circumstances under which such a selected procedure may be undertaken. By this method I have been able to define all dermatomes of the lower extremity and one dermatome of the upper extremity, namely the sixth cervical. In order to fill up the gap and to define the other cervical and the thoracic dermatomes we can use a method which I should like to call "the constructive method." It is obvious that when a series of contiguous roots is divided, the superior border of the resulting anæsthesia represents the inferior border of the dermatome which corresponds to the next higher intact root, while the inferior border of the anæsthetic area represents the superior border of the next lower dermatome. By such observations I have been able to map out nearly all dermatomes in man.



A. B.

Fig. 5.—Head's scheme of the dermatomes in man.

The other method which I have used for the definition of dermatomes is based upon the fact, first demonstrated by Stricker and Bayliss on animals, that faradic stimulation of the distal part of a divided posterior root is followed by vaso-dilatation. I have found the same in man. I have also observed that the vaso-dilatation following the electrical stimulation of a single posterior root is limited to a sharply circumscribed area similar in shape and situation to the dermatome as defined by means of the isolation method.

I have obtained vaso-dilatation by stimulation of nearly all cervical, thoracic, lumbar and sacral posterior roots. The area of vaso-dilatation resulting from the electrical stimulation of a single posterior root is not absolutely identical with the area of remaining sensibility; it is smaller and approximates in its extent much more to the area of herpetic eruption mapped out by Head.

For a long time it has been an open question whether the vaso-dilatation following faradic stimulation of a posterior root is due to antidromic conduction along the afferent nerve-fibres, as Bayliss believed, or whether it is the effect of stimulation of efferent fibres arising in the cord and passing outward by the posterior roots. In eight cases in which I had divided posterior roots in men we found a number of myelinated fibres preserved in the central part of the divided root. The root resection was performed in one of my cases five years before death (fig. 6), and in another four and a half years before death. The fact that these fibres are preserved after the root had been totally divided proves that their ganglion cells do not lie in the spinal ganglia but in the cord, and that these fibres are really efferent. The calibre of these fibres is very fine as compared with the thick myelinated sensory fibres of the posterior root (figs. 7 and 8.) The results of these anatomical investigations prove, I believe, that the posterior roots carry, in addition to sensory fibres, efferent fibres and it seems to me admissible to assume that the vaso-dilatation following the electrical stimulation of a posterior root is the result of the stimulation of these efferent fibres.

After this short review of the methods of defining the dermatomes in man I shall describe the special dermatomery. I begin with the dermatomes of the lower extremity.

## LUMBAR AND SACRAL DERMATOMES.

*First lumbar dermatome.*—The first lumbar dermatome, that is the area of sensibility which remains after the eleventh and twelfth thoracic and the second to the fifth lumbar and all sacral roots having been divided, the first lumbar root alone being left intact, occupies the inferior part of the abdomen and the upper part of the anterior and lateral

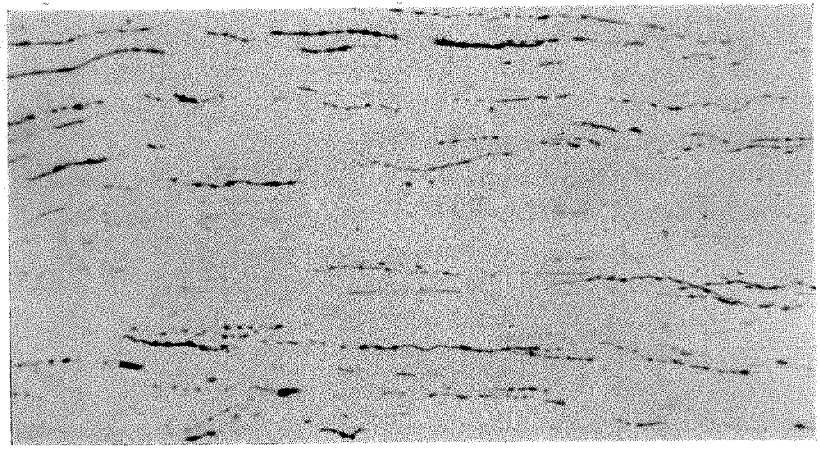


FIG. 6.

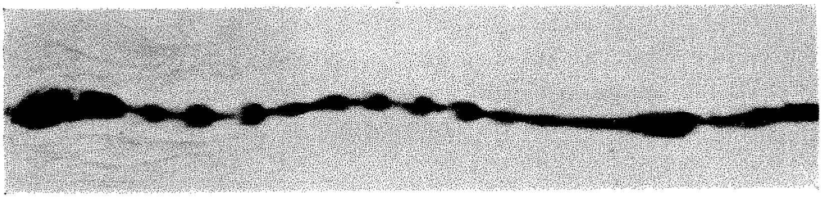


FIG. 7.

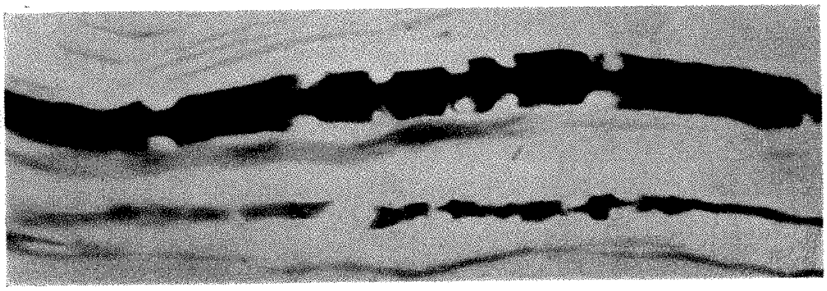


FIG. 8.

FIG. 6.—Efferent myelinated fibres of the central part of a divided posterior root, 4½ years after resection.

FIG. 7.—A single myelinated efferent fibre of a posterior root; note its fine calibre.

FIG. 8.—A single myelinated sensory fibre of a posterior root; note its thick calibre.

surfaces of the leg. At the dorsal side it forms a band, which reaches the spine of the fifth lumbar vertebra (figs. 9 and 10). This area of remaining sensibility is very similar to the area outlined by Head (fig. 5), but exceeds it to some extent, especially above its superior border. The extent of the herpetic eruption in a case of herpes of the first lumbar ganglion is shown in fig. 11.

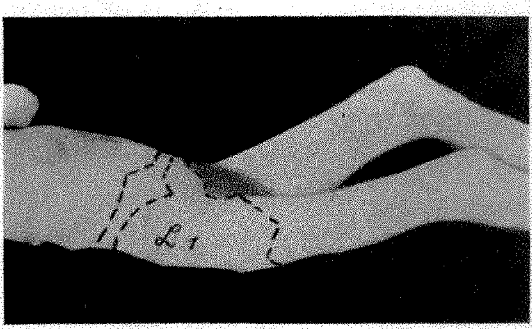


FIG. 9.

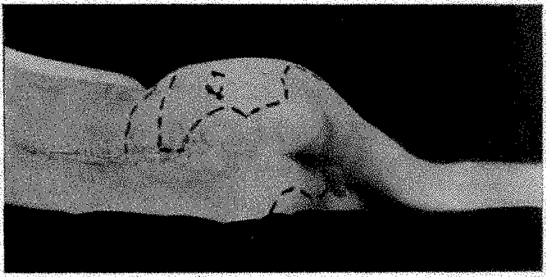


FIG. 10.

**FIGS. 9 and 10.—The 1st lumbar dermatome defined by remaining sensibility after resection of 11th and 12th thoracic, and 2nd to 5th lumbar and 1st to 5th sacral roots.**

The constructive method defines the same borders for the first lumbar dermatome. In a case in which the eighth, ninth, tenth, eleventh and twelfth thoracic roots were resected, the inferior border of the anæsthesia, shown in fig. 12, represents the superior border of the first lumbar dermatome; it conforms to the superior border of the remaining sensibility in the case described above. In another case, in which the second, third, fourth and fifth lumbar and all sacral roots were divided, the superior border of the anæsthesia shown in figs. 13 and 14 was practically identical with the inferior border of the remaining sensibility in the case illustrated in figs. 9, 10. In a case of division of the second and third lumbar roots the superior border of the anæsthesia was similar to that of the preceding cases on the anterior aspect of the leg, but on the posterior aspect there was no anæsthesia, the sacral roots having been left intact (figs. 15, 16).

*Second lumbar dermatome* was defined by the isolation method in a case in which the twelfth thoracic and the first lumbar, as well as the third, fourth and fifth lumbar and all sacral roots were divided (fig 17).

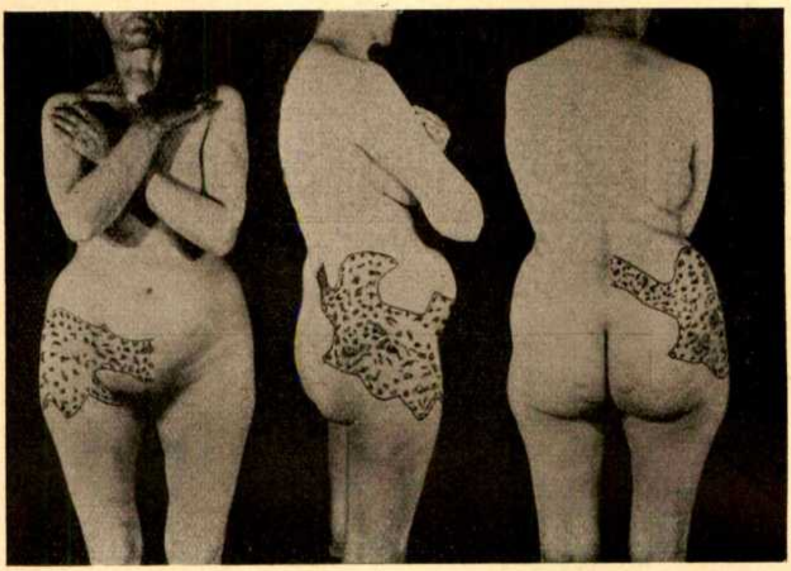


FIG. 11.—Herpes zoster of the 1st lumbar ganglion.

It lies chiefly on the anterior aspect of the thigh, but there is also a small band on the dorsum of the trunk which is not continuous with the main area upon the anterior surface of the leg (fig. 18). We find exactly the same distribution in Head's scheme (fig. 5).

The constructive method demonstrates the same borders for the second lumbar dermatome. In a case in which the third, fourth and fifth lumbar roots and the first sacral root were divided, the superior border of the anæsthesia corresponds to the inferior border of the second lumbar dermatome (fig. 19), and in a case of resection of the eleventh and twelfth thoracic and the first lumbar roots the inferior border of the anæsthesia represents the superior border of the second lumbar dermatome (fig. 20).

*Third lumbar dermatome.*—The third lumbar dermatome was outlined by the isolation method on the other leg of the same patient as the second lumbar dermatome (fig. 17). On comparison of the legs the great extent of overlap becomes evident. The third lumbar dermatome has a characteristic shape; a central part around the knee, an upper prolongation along the anterior and internal surface of the thigh, and an inferior strip or band along the inner side of the leg reaching below as far as the internal malleolus. There is also a small band on the dorsal aspect of the trunk, which is not in continuity with the main area upon the lower limb (fig. 18). Fig. 21 shows the third lumbar dermatome in another case. On comparing these cases it is seen that the extent of the same dermatome may present considerable individual variations. It is noteworthy that in the case represented by fig. 21 the first sacral dermatome, which was also defined, had an unusually large extension. The situation and the extent of the third lumbar dermatome according to Head is shown in fig. 5.

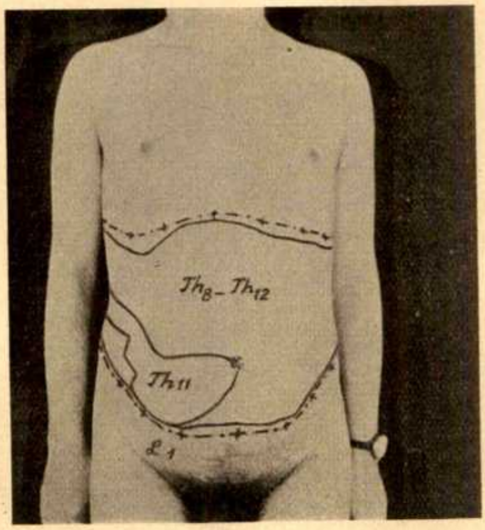


FIG. 12.—The superior border of the 1st lumbar dermatome; resection of 8th to 12th thoracic roots.

The constructive method confirms the results obtained by the isolation method. In a case in which all the roots between the ninth thoracic and the second lumbar were divided, the inferior border of the anæsthetic area corresponds exactly with the superior border of the dermatome demonstrated above by the isolation method (fig. 22); and

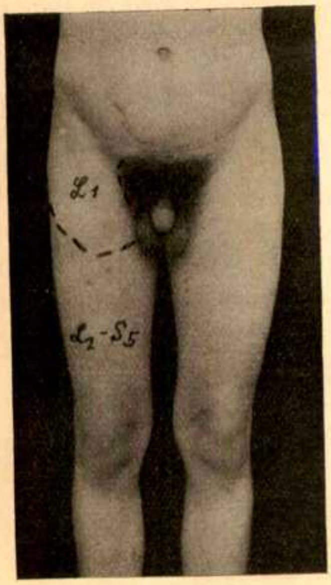


FIG. 13.

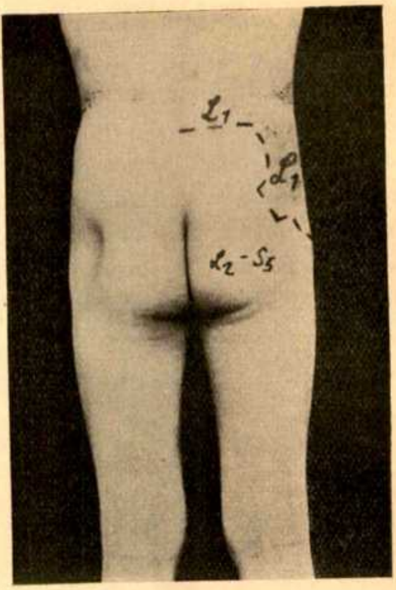


FIG. 14.

FIGS. 13 and 14.—The inferior border of the 1st lumbar dermatome; resection of 2nd to 5th lumbar and 1st to 5th sacral roots.

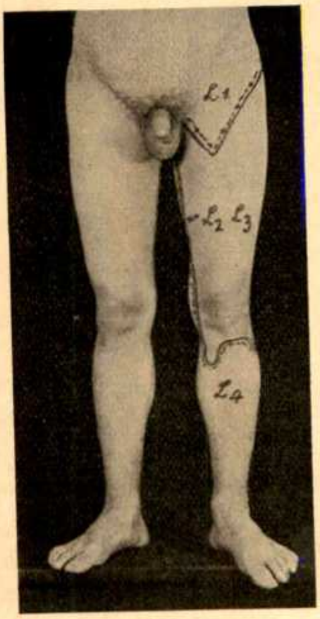


FIG. 15.

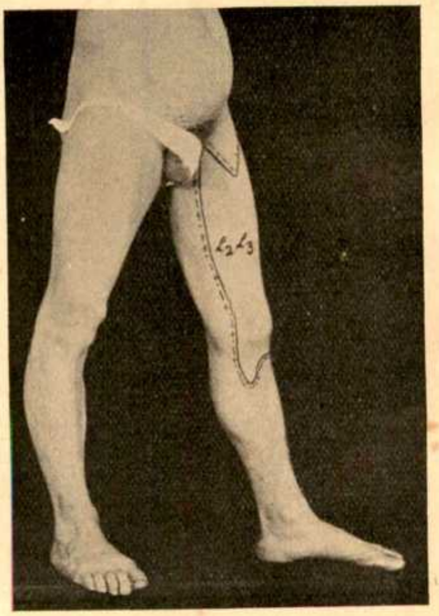


FIG. 16.

FIGS. 15 and 16.—The inferior border of the 1st lumbar dermatome; resection of 2nd and 3rd lumbar roots.

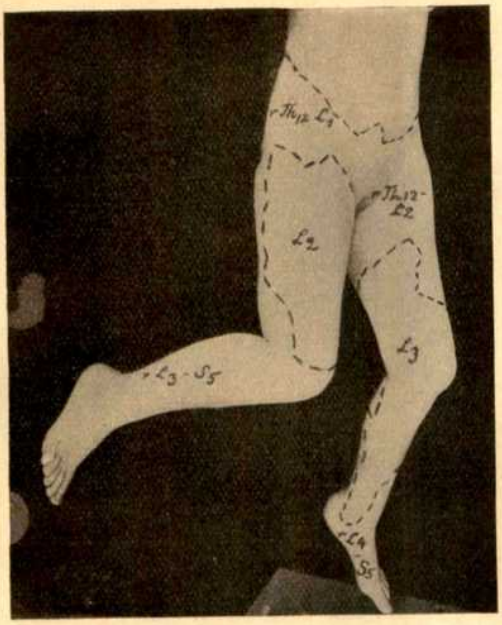


FIG. 17.

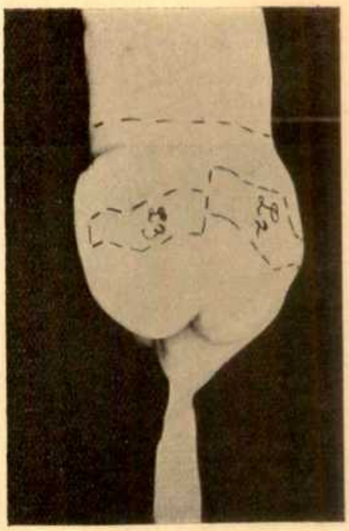


FIG. 18.

FIGS. 17 and 18.—The 2nd lumbar dermatome; resection of Th12 and L1, and L3 to S5 on the right side. The 3rd lumbar dermatome; resection of Th12, L1 and L2, and L4 to S5 on the left side.

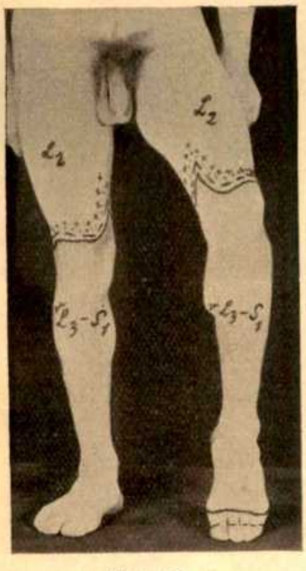


FIG. 19.

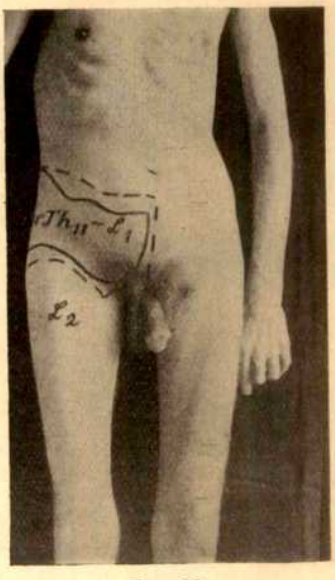


FIG. 20.

FIG. 19.—The inferior border of the 2nd lumbar dermatome; resection of L3 to S1.

FIG. 20.—The superior border of the 2nd lumbar dermatome; resection of Th11, Th12 and L1.

in another case in which the fourth and fifth lumbar and all sacral roots were divided, the superior border of the anæsthesia runs along the anterior side of the tibia down to the internal malleolus and then upwards along the internal side of the leg (figs. 23 and 24).

The area of vaso-dilatation following electrical stimulation of the third lumbar root (fig. 25) also coincides in situation and shape with the dermatome defined by the isolation method, but its extent is not quite as large as that of the area of remaining sensibility.

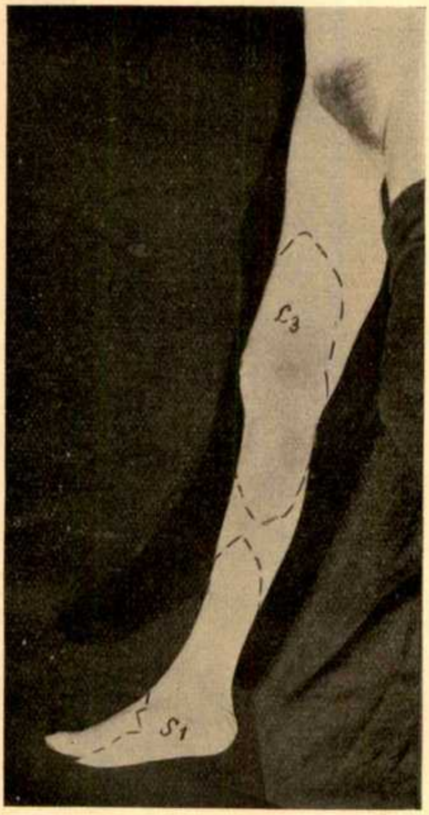


FIG. 21.

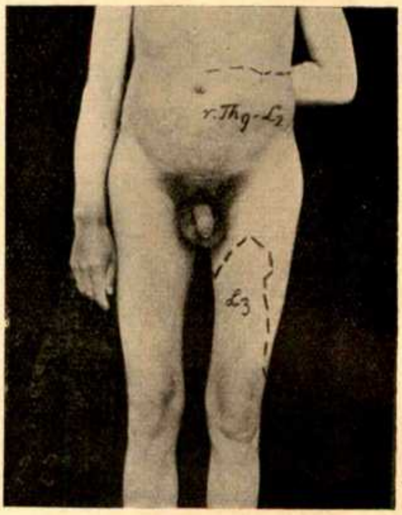


FIG. 22.

FIG. 21.—The 3rd lumbar dermatome of relatively small extent. The 1st sacral dermatome of large extent. Resection of Th11 to L2, L4 and L5, S2 to S5.

FIG. 22.—The superior border of the 3rd lumbar dermatome; resection of Th9 to L2.

*Fourth lumbar dermatome* occupies the anterior side of the leg, the internal part of the dorsum of the foot and the great toe (fig. 26). On the sole its border runs from between the first and second toes backwards behind the internal malleolus (fig. 27), and upwards along the posterior-internal side of the leg. At the level of the knee it turns forwards, then bends behind the head of the fibula to the outer side of the leg (fig. 28) and finally returns to the dorsal aspect of the foot where it reaches the interdigital space between the hallux and the second toe.

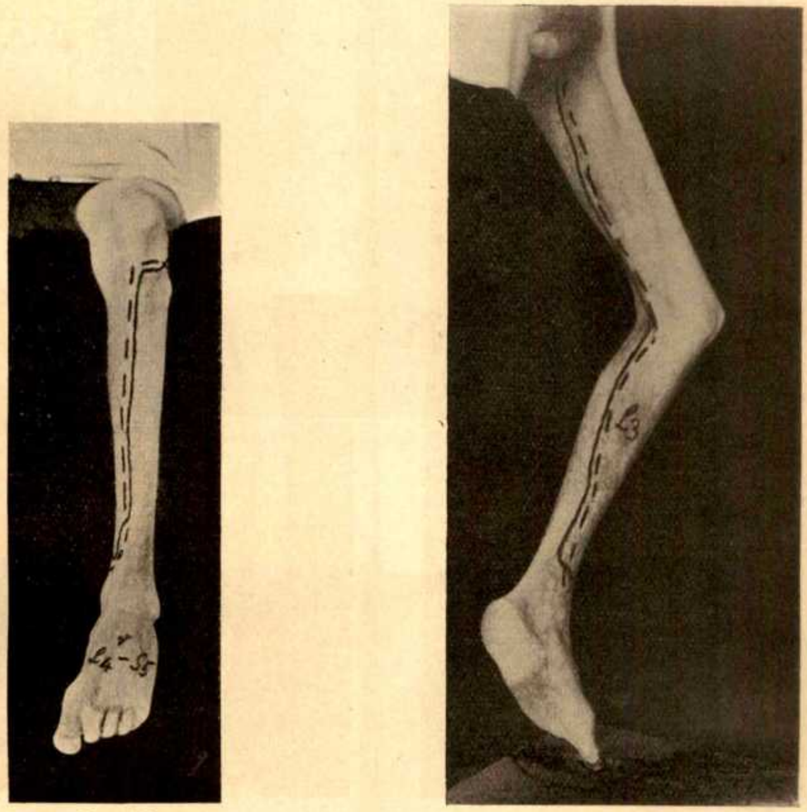


FIG. 23. FIG. 24.

FIGS 23 and 24.—The inferior border of the 3rd lumbar dermatome; resection of L4 to S5.

In the second case the situation, shape and extension of the fourth lumbar dermatome were almost identical (figs. 29, 30 and 31). In a third case the extent was very similar (figs. 32 and 25). The photograph (fig. 25) shows the large overlap of the fourth and the third lumbar dermatomes, the latter of which was outlined by the vaso-dilatation excited by faradic stimulation of the third lumbar root. The topography of the fourth lumbar dermatome in a fourth case is shown in fig. 33.

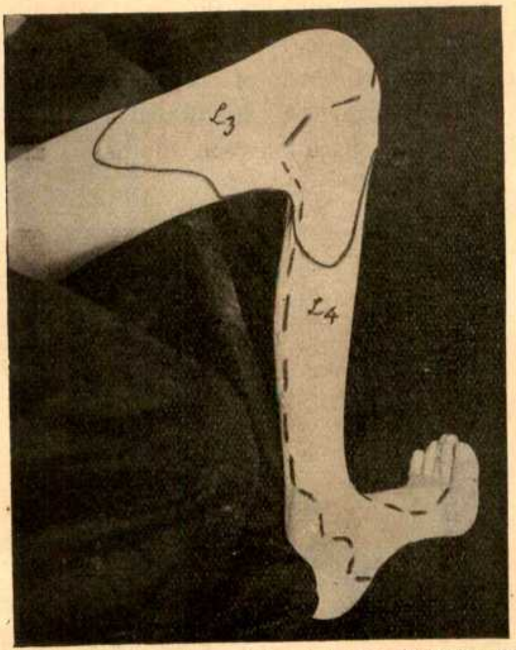


FIG. 25.—The 3rd lumbar dermatome defined by vasodilatation following electrical stimulation of 3rd posterior lumbar root. The 4th lumbar dermatome defined in the same case by remaining sensibility after resection of all lumbar and sacral roots except the 4th lumbar. The continuous line represents the border of the 3rd dermatome, the broken line that of the 4th lumbar dermatome.

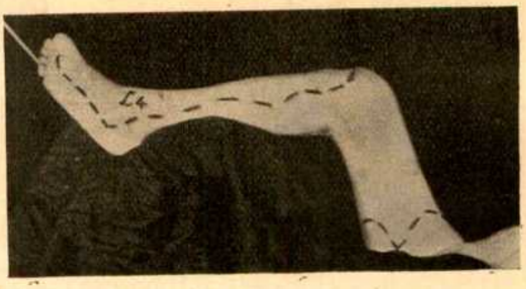


FIG. 27.

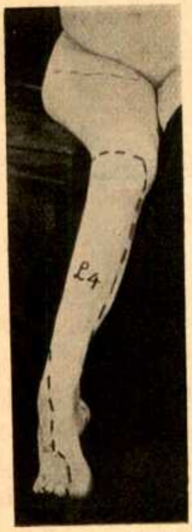


FIG. 26.

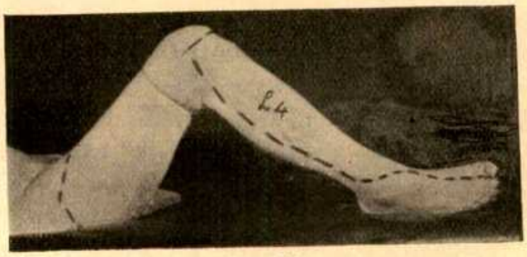


FIG. 28.

FIGS. 26, 27 and 28.—The 4th lumbar dermatome; resection of L2 and L3, and L5 to S5.

The fourth lumbar dermatome, as defined by the isolation method, has a markedly larger extent than Head determined. In Head's scheme the big toe is not included in it.

*The fifth lumbar dermatome* occupies the anterior side of the leg, the entire dorsum of the foot and of all toes (figs. 34, 35 and 36). The border runs along the outer border of the foot behind the external malleolus, up the leg and then turns below the head of the fibula to the anterior aspect, from where it runs down along the internal side of the leg to the sole. The dermatome occupies the medial part of the sole, and the plantar surfaces of the first, second and third toes, but not that of the fourth and fifth toes (fig. 37).

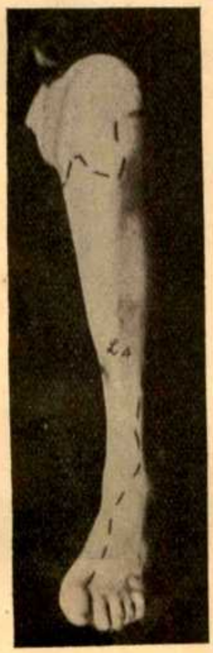


FIG. 29.

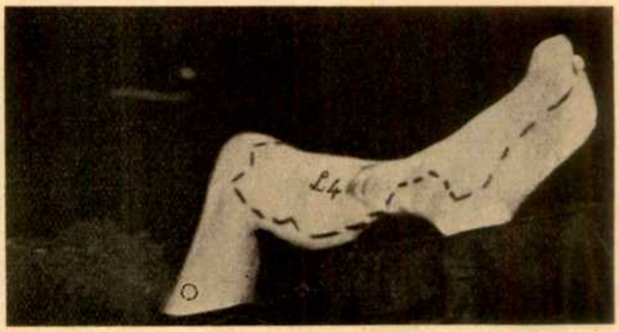


FIG. 30.

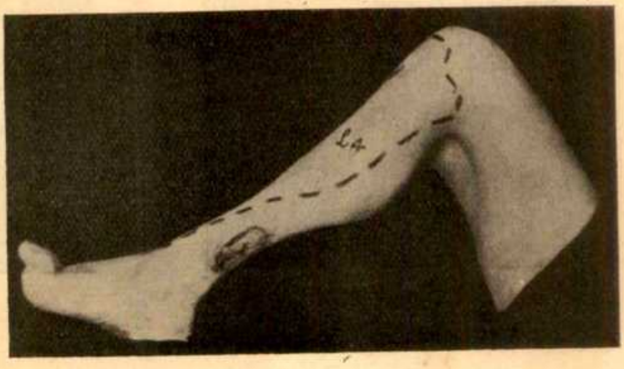


FIG. 31.

FIGS. 29, 30 and 31.—The 4th lumbar dermatome in a second case; resection of L2 and L3, and L5 to S5.

The constructive method reveals the same borders for the fifth lumbar dermatome. In a case in which I resected the first, second and third sacral roots, the anæsthetic area on the posterior side is shown in fig. 38. Its border runs along the external side of the foot, but the medial half of the sole and the first, second and third toes preserved their sensibility (fig. 39). In this photograph the continuous line indicates the limits of tactile anæsthesia, the broken line that of the analgesia; the extent of the latter is larger than that of the former. This is common in cases of root resection, and corresponds with the fact, pointed out by Sherrington, that the tactile dermatomes are larger than the pain dermatomes.

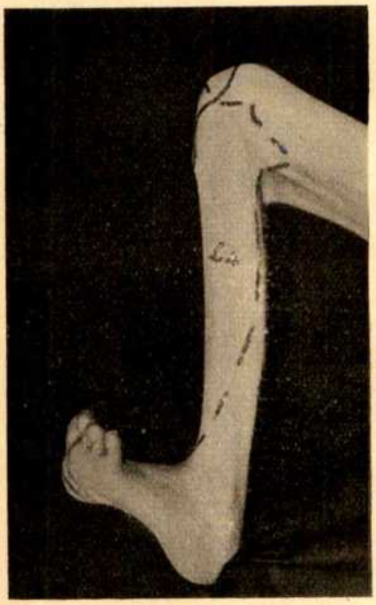


FIG. 32.

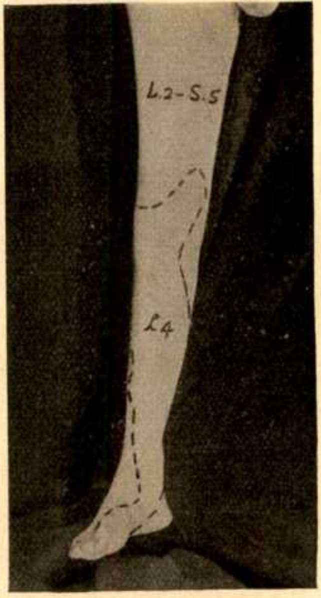


FIG. 33.

FIG. 32.—The 4th lumbar dermatome in a third case; resection of L2 and L3, and L5 to S5.

FIG. 33.—The 4th lumbar dermatome in a fourth case; resection of L2 and L3, and L5 to S5.

*The first sacral dermatome* occupies the sole and the plantar surfaces of the toes (fig. 40); in some cases it extends even to the dorsal surfaces of the toes. From the sole the dermatome spreads upwards along the posterior side of the leg (fig. 41). The size and shape of the first sacral dermatome, as defined by the isolation method, are very similar to the first sacral dermatome in Head's scheme (fig. 5).

*The second sacral dermatome* occupies the posterior surface of the thigh and of the leg, the sole of the foot and the plantar aspects of the toes (fig. 42). In another case the second sacral dermatome extended on to the dorsal surfaces of the toes (fig. 19). The extent of the remaining sensibility in my cases was considerably larger than the area of the second sacral dermatome in Head's scheme (fig. 5).

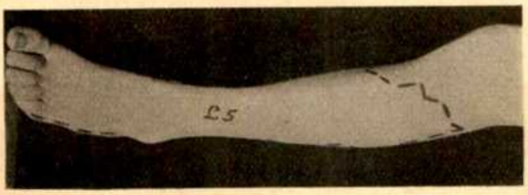


FIG. 34.

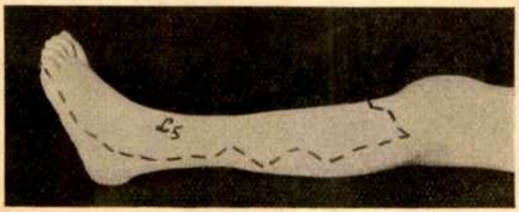


FIG. 35.

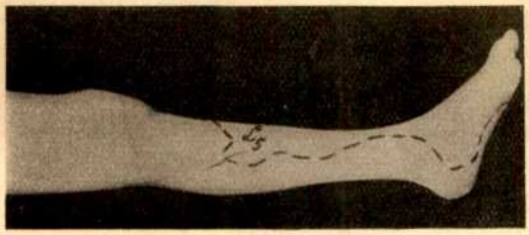


FIG. 36.

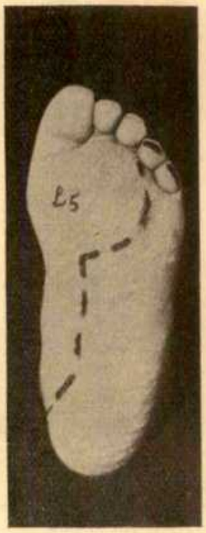


FIG. 37.

FIGS. 34, 35, 36 and 37.—The 5th lumbar dermatome ; resection of Th12 to L4, and S1 to S5.

## THORACIC DERMATOMES.

I have had no opportunity of defining the different thoracic dermatomes by the isolation method, but the constructive method has furnished all the details necessary for determining the inferior and superior borders of practically all of them. A full description of all these separate dermatomes is not necessary ; their distribution and size can be seen in the diagram which I have worked out from the examination of a great number of cases of division of posterior thoracic roots (fig. 43). A few details are, however, worthy of notice.

The tenth thoracic dermatome has a typical situation around the umbilicus, and the superior border of the eleventh and the inferior border of the ninth thoracic dermatomes extend just to it. The mammilla lies within the fifth thoracic dermatome, and the inferior border of the fourth and the superior border of the sixth reach to a horizontal line through it.

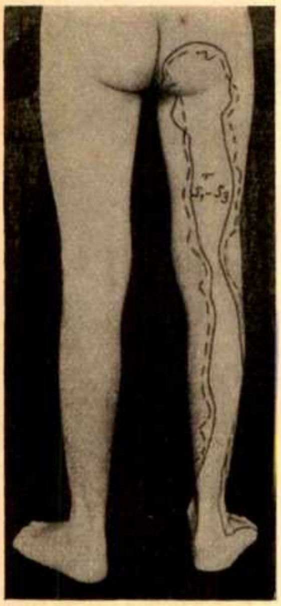


FIG. 38.

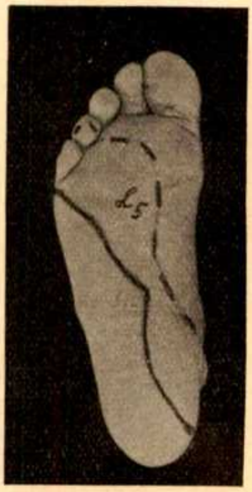


FIG. 39.

FIGS. 38 and 39.—The anæsthesia following resection of S1, S2 and S3, showing the border of the 5th lumbar dermatome on the planta pedis; the tactile dermatome (continuous line) is of larger extent than pain dermatome (broken line).

The thoracic dermatomes, as defined by the vasodilatation excited by electrical stimulation of the posterior thoracic roots, conform closely to the areas obtained by the constructive method (figs. 12, 44, 45, 46, 47, 48, 49, 50).

The area of vasodilatation following faradic stimulation of the third thoracic root includes a triangular patch in the axilla. In the case represented by fig. 51 the latter was not continuous with the main area upon the thorax. I have found this lack of continuity of the areas of vasodilatation following electrical stimulation of the posterior roots in a good many other cases.

In another case the triangular area in the axilla was not so large (fig. 52); there exist undoubtedly considerable individual variations in it. A similar triangular prolongation of the third thoracic dermatome into the axilla is demonstrable by the constructive method, as after division of the first and second thoracic roots the area of resulting anæsthesia shows the characteristic indentation due to its prolongation into the axilla (fig. 53). In another case of resection of the first and second thoracic roots the characteristic triangular prolongation of the third thoracic dermatome also is visible (fig. 54), and in another patient in whom the second and first thoracic, and the eighth and seventh cervical roots were resected, the triangular prolongation of the third thoracic dermatome into the axilla comes out very clearly (fig. 55).

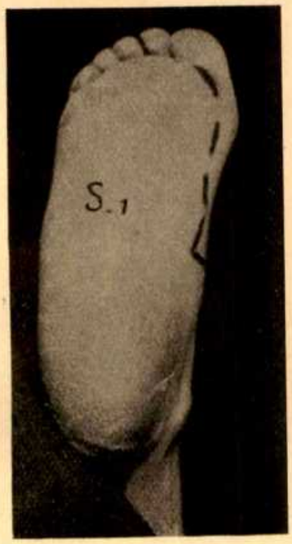


FIG. 40.

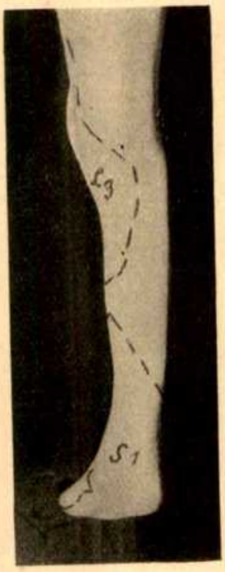


FIG. 41.

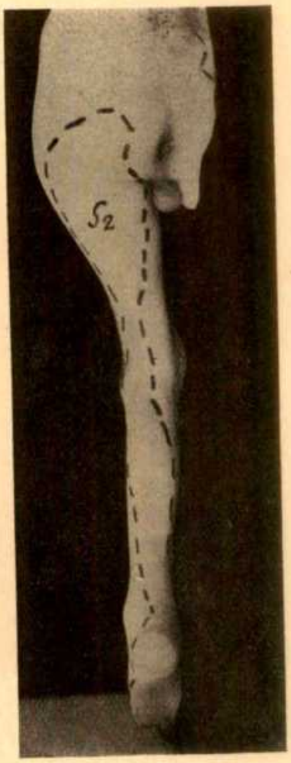


FIG. 42.

FIGS. 40 and 41.—The 1st sacral dermatome and the 3rd lumbar dermatome; resection of Th11 to L2, L4 and L5, and S2 to S5. Compare fig. 21.

FIG. 42.—The 2nd sacral dermatome; resection of Th11 to S1, and S3 to S5.

Sometimes this triangular prolongation of the third thoracic dermatome extends even further down the arm, as in a case of resection of the second and first thoracic roots and the fifth to the eighth cervical roots reported by Head (fig. 56). In this case the triangular area of remaining sensibility resembles closely in size and shape the triangular prolongation delimited by the area of vaso-dilatation produced by electrical stimulation of the third thoracic root, which is shown in one of the illustrations (fig. 51).

*The second thoracic dermatome*, as represented by the area of vaso-dilatation excited by faradic stimulation of the second thoracic root, occupies the inner side of the arm. It extends downwards as far as the internal condyle of the humerus, and it is prolonged on to the anterior and posterior surfaces of the thorax (figs. 57, 58). In the case illustrated by fig. 58, vaso-dilatation reached as far as the wrist; this was due to the fact that the fibres of the first thoracic dermatome were also stimulated in consequence of an anastomosis between the second and the first thoracic roots. The two bands of the second thoracic dermatome which extend on to the thorax from the inner side of the arm form a characteristic angle (fig. 58c), and consequently in all cases of division of the third, fourth and fifth thoracic roots the anæsthesia includes a triangular extension into the axilla (fig. 59).

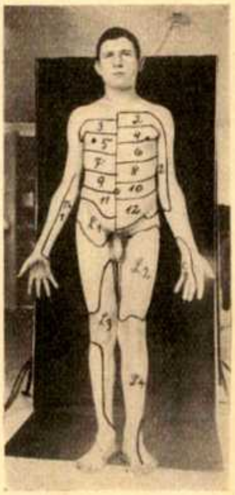
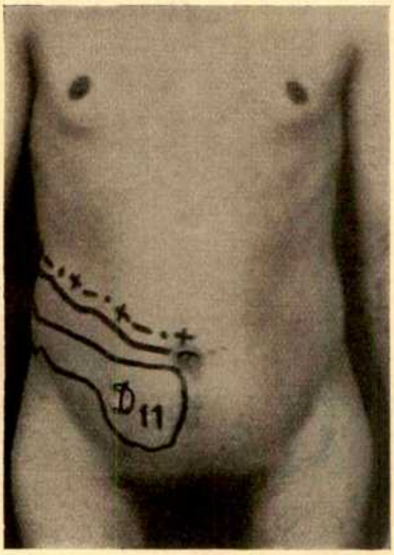


FIG. 43.

FIG. 43.—Scheme of thoracic dermatomes.



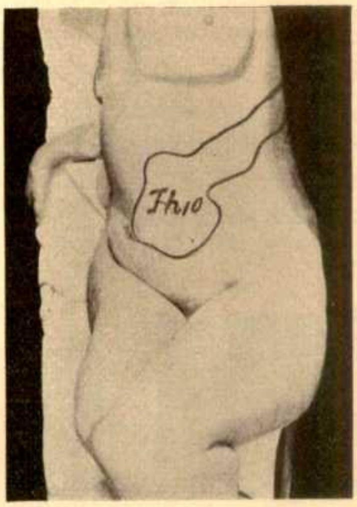
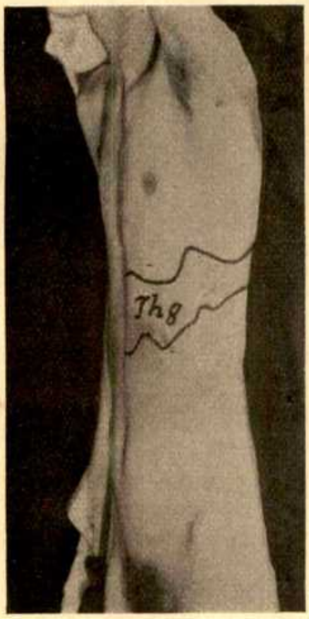


FIG. 44.

FIG. 45.

FIG. 44.—The 11th thoracic dermatome defined by vasodilatation; resection of Th10 to S5.

FIG. 45.—The 10th thoracic dermatome defined by vasodilatation.



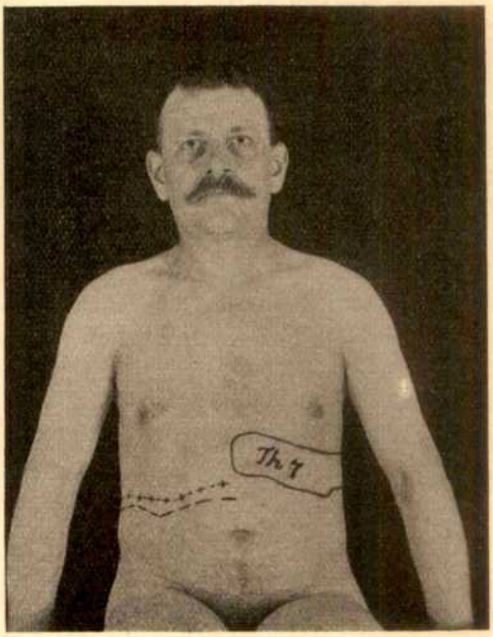


FIG. 46.

FIG. 47.

FIG. 46.—The 8th thoracic dermatome defined by vasodilatation.

FIG. 47.—The 7th thoracic dermatome defined by vasodilatation.

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*The first thoracic dermatome*, as represented by the area of vasodilatation following electrical stimulation of the first thoracic root, occupies the internal side of the fore-arm as far down as the wrist (fig. 57). Unfortunately the superior border of this dermatome could not be mapped out in this case, since the second thoracic root had been stimulated just before and the effect of this stimulation, which always lasts a considerable time, had not disappeared when the first thoracic root was stimulated.

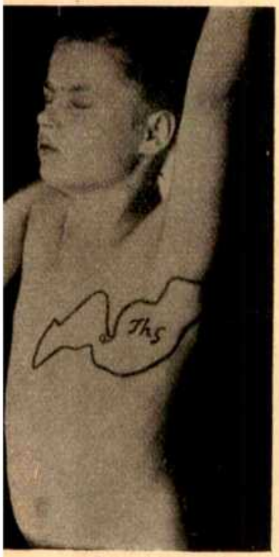


FIG. 48.

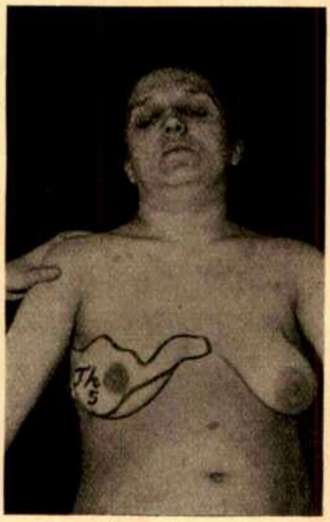


FIG. 49.

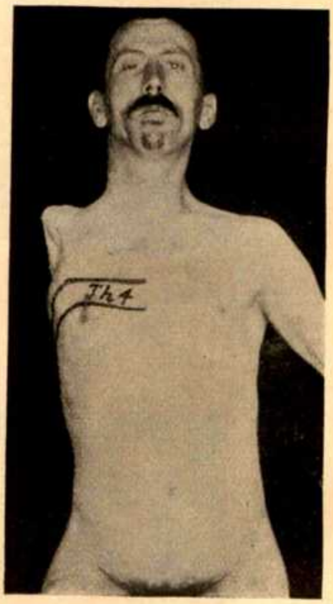


FIG. 50.

FIGS. 48 and 49.—The 5th thoracic dermatome defined by vasodilatation.
FIG. 50.—The 4th thoracic dermatome defined by vasodilatation.

That the second thoracic root, and probably the first thoracic root as well, take part in the innervation of the thorax, is demonstrated by the fact that after resection of the first and second thoracic roots a small band of anæsthesia is, in some cases, found on the thorax (fig. 60).

## CERVICAL DERMATOMES.

*The eighth cervical dermatome*, as represented by the area of vasodilatation following electrical stimulation of the eighth cervical root, occupies the fifth and fourth fingers, the ulnar half of the third finger,

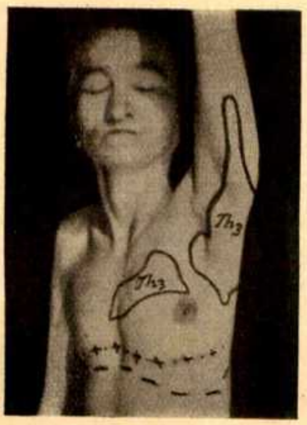


FIG. 51.

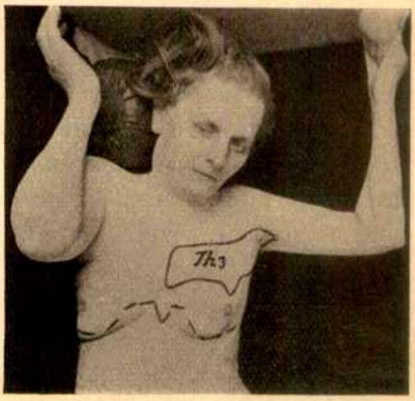


FIG. 52.

FIG. 51.—The 3rd thoracic dermatome defined by vasodilatation.

FIG. 52.—The 3rd thoracic dermatome defined by vasodilatation.

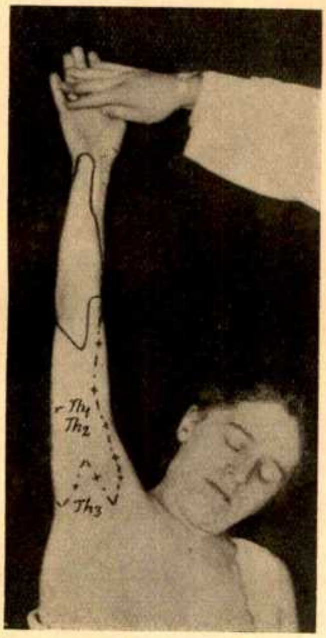


FIG. 53.

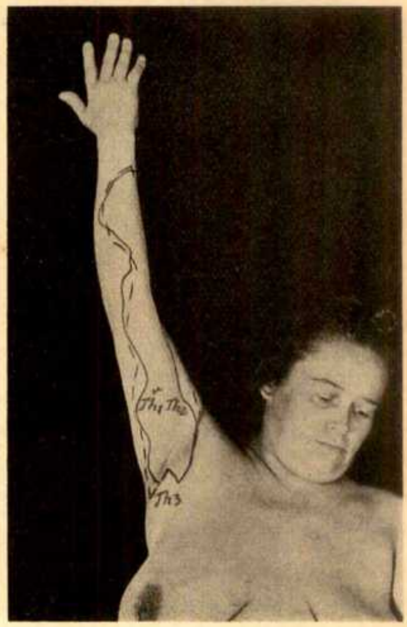


FIG. 54.

FIG. 53.—Anæsthesia following resection of Th1 and Th2 with the characteristic indentation of the 3rd thoracic dermatome in the axilla. Note the considerably larger extent of analgesia and thermanæsthesia + –. + –., than that of the tactile anæsthesia, ———.

FIG. 54.—Anæsthesia following resection of Th1 and Th2; indentation by the 3rd thoracic dermatome in the axilla. Analgesia and tactile anæsthesia of about the same extent.

the ulnar part of the hand and to some extent the distal part of the fore-arm (fig. 61). The overlap of the eighth cervical dermatome on the fore-arm is demonstrated by a case in which the first and second thoracic roots had been resected; the inferior border of the anæsthesia does not reach as far as the wrist (fig. 62), and the sensibility preserved on the lower part of the fore-arm must be due to extension of the eighth cervical dermatome to the fore-arm. Individual variations in the distribution of the eighth cervical dermatome exist however, for in another case of resection of the first and second thoracic roots, already demonstrated above, the anæsthesia reached distalwards as far as the wrist (fig. 53).

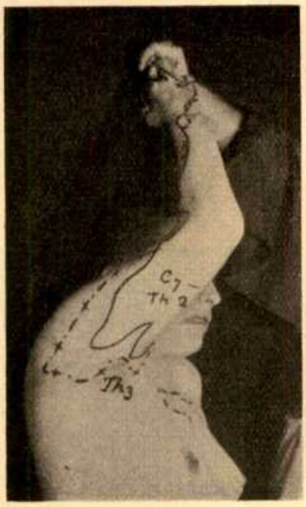


FIG. 55.

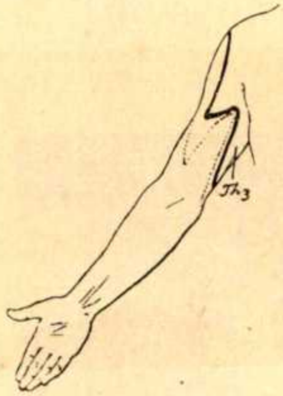


FIG. 56.

FIG. 55.—Anæsthesia following resection of C7, C8, Th1 and Th2, with characteristic indentation by the 3rd thoracic dermatome in the axilla. Analgesia and thermanæsthesia + –. + –. of larger extent than tactile anæsthesia, ———.

FIG. 56.—Tactile anæsthesia ...... and analgesia ——— following resection of C5 to Th2 reported by Head. The 3rd thoracic dermatome occupies the internal surface of upper arm.

I have no cases affording landmarks for the definition of the seventh cervical dermatome.

*The sixth cervical dermatome*, outlined by the remaining sensibility after resection of the first and second thoracic, and the eighth, seventh, fifth and fourth cervical roots, occupies the thumb, the index finger and the thenar eminence, and extends up the external side of the fore-arm and of the upper arm (figs. 63, 64). The tactile dermatome is considerably larger than the pain dermatome.

In all cases in which the first, second, third, fourth and fifth cervical roots are divided, the inferior border of the anæsthesia outlines a triangular flap below the shoulder (fig. 65). The borders of this area represent the superior limits of the sixth and seventh cervical dermatomes.

*The fifth cervical dermatome*, as shown by the vaso-dilatation following stimulation of the fifth cervical root, covers a large area. It reaches from the shoulder along the lateral side of the arm downwards as far as the thumb (figs. 66, 67, 68). The same case demonstrates very well the large overlap of the fifth cervical dermatome with the sixth and seventh dermatomes; the first, second, third, fourth and fifth cervical roots were resected, but the resulting anæsthesia does not extend further downwards than about 6 cm. below the shoulder; on the other hand the fifth dermatome reaches as far as the thumb.

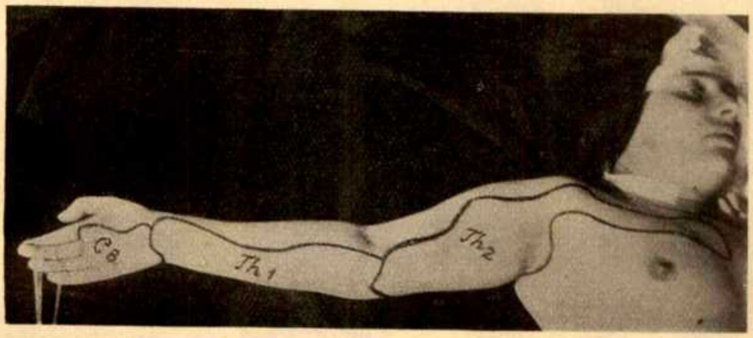
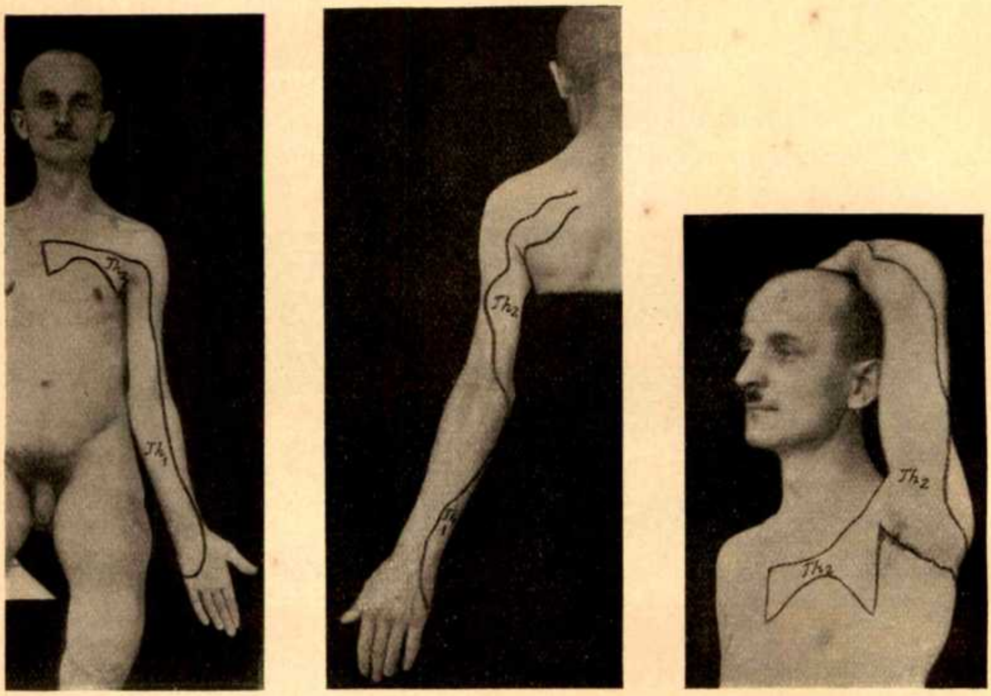


FIG. 57.—The 2nd and 1st thoracic and 8th cervical dermatomes defined by vaso-dilatation. The 1st thoracic and the 8th cervical dermatomes do not show their full extent.

*The fourth cervical dermatome.*—The inferior border of the area of vaso-dilatation following electrical stimulation of the fourth cervical root is shown in fig. 69. Its superior border could not be outlined in this case as the skin of the neck had been coloured by a solution of iodine. In this case the first, second, third and fourth cervical roots were resected. Fig. 70 shows that the area of vaso-dilatation produced by faradic stimulation of the fourth cervical root extends much lower than the inferior border of the area of anæsthesia following the resection of the first to fourth cervical roots. This shows clearly the amount of overlap of the fourth cervical dermatome with the fifth, sixth and seventh cervical dermatomes and the first and second thoracic.

The constructive method confirms the result obtained by the electrical stimulation of the fourth cervical root. In a case (figs. 71 and 72) in which the fifth, sixth, seventh and eighth cervical, and the first, second and third thoracic roots were divided, the characteristic triangular area of the fourth cervical dermatome may be seen at the superior border of the resulting anæsthesia.



A B C

FIG. 58.—The 2nd and 1st thoracic dermatomes defined by vasodilatation.

In a case reported by Cushing, in which the second and third cervical roots were resected, the inferior border of the anæsthesia marks the superior border of the fourth cervical dermatome (fig. 73). My own cases of resection of the second and third cervical roots demonstrate a similar inferior border of the anæsthesia (figs. 74, 75). The analgesia occupies a larger area than the tactile anæsthesia, that is to say the pain dermatome is considerably smaller than the tactile. The difference between the extent of analgesia and that of tactile anæsthesia is still greater in another case in which the second and third cervical roots were resected (figs. 76, 77); the area of anæsthesia is exceptionally small, but the inferior border of the analgesia and thermanæsthesia conforms to Cushing's observations.

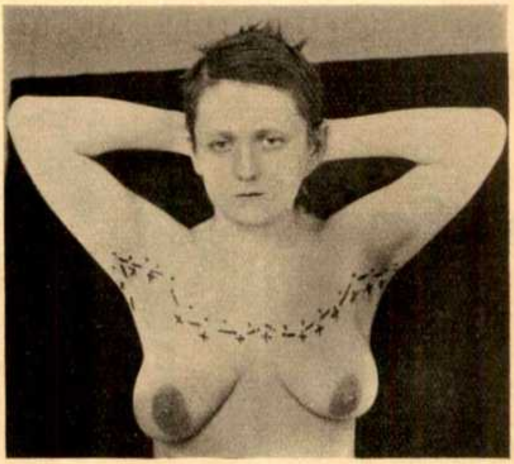


FIG. 59.—The superior border of the anæsthesia in a case of chordotomy interrupting the pain and thermal fibres corresponding to the 3rd, 4th, 5th and 6th and lower thoracic roots.

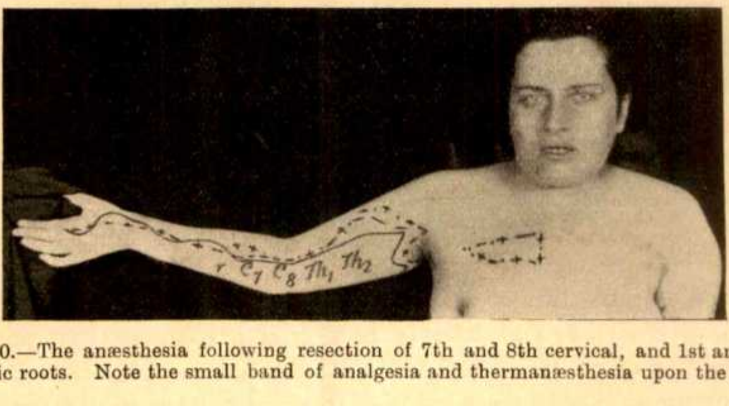


FIG. 60.—The anæsthesia following resection of 7th and 8th cervical, and 1st and 2nd thoracic roots. Note the small band of analgesia and thermanæsthesia upon the chest.

*The third cervical dermatome*, as represented by the area of vasodilatation following electrical stimulation of the third cervical root, is shown in fig. 78. It reaches upwards to the mandible, includes the ear and extends downwards as far as the clavicle. In the same case the fifth cervical root also was stimulated, and it can be seen how closely the two areas of vasodilatation come together.

The inferior border of the third cervical dermatome was also defined by resection of the fifth and the fourth cervical roots (fig. 79). The case is interesting in as far as there was no tactile anæsthesia ; the resection of the two roots produced analgesia and thermanæsthesia only, further evidence of the larger extent of the tactile than of pain and thermal dermatomes. In another case in which the fourth, fifth, sixth, seventh and eighth cervical and the first to the fifth thoracic roots were resected the lower border of the third cervical dermatome was similar (fig. 80), but sometimes the third cervical dermatome extended further downwards, as in a case in which the fourth, fifth, sixth, seventh and eighth cervical and the first to the fourth thoracic roots were resected (fig. 81). This case demonstrates again the considerable individual variations in the extent of a single dermatome.

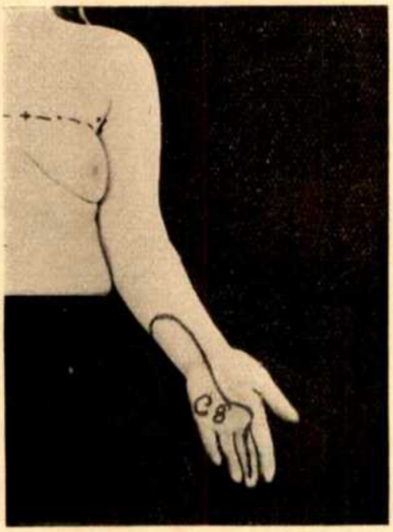


FIG. 61.

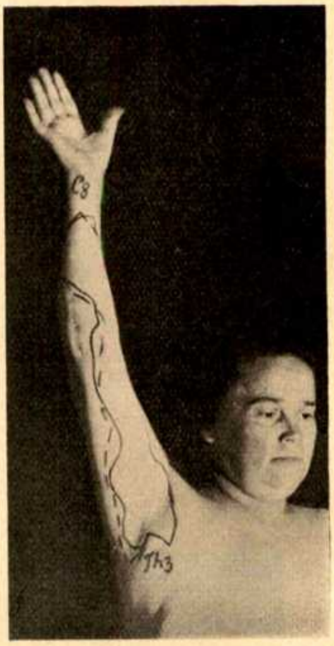


FIG. 62.

FIG. 61.—The 8th cervical dermatome defined by vasodilatation.

FIG. 62.—Anæsthesia following resection of Th1 and Th2. Note the conservation of sensibility in the anterior part of the fore-arm. Compare fig. 54.

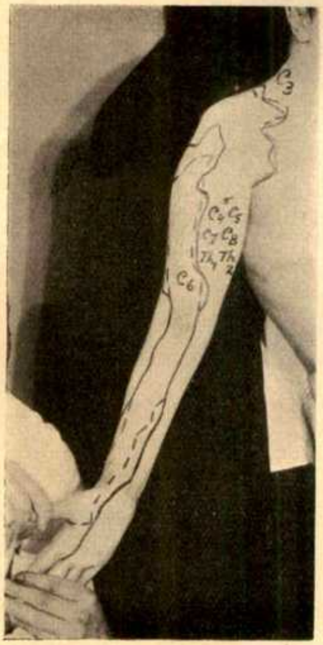


FIG. 63.

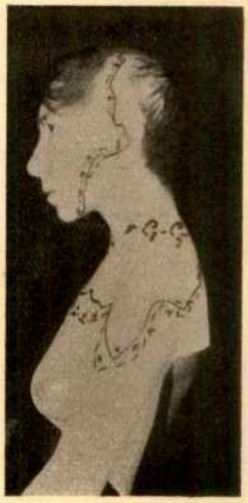


FIG. 65.

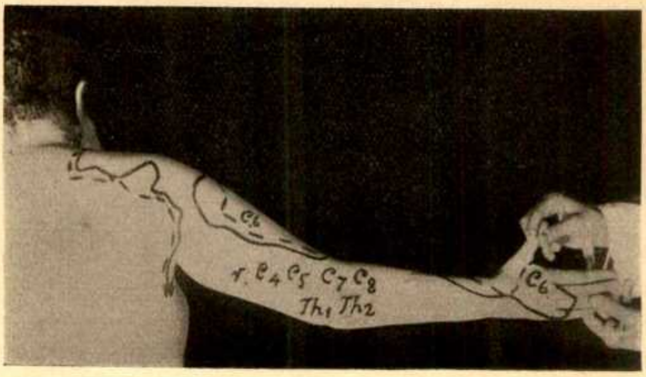


FIG. 64.

FIGS. 63 and 64.—The 6th cervical dermatome; resection of C4 and C5, and of C7 to Th2.

FIG. 65.—The anæsthesia following resection of C1 to C5.

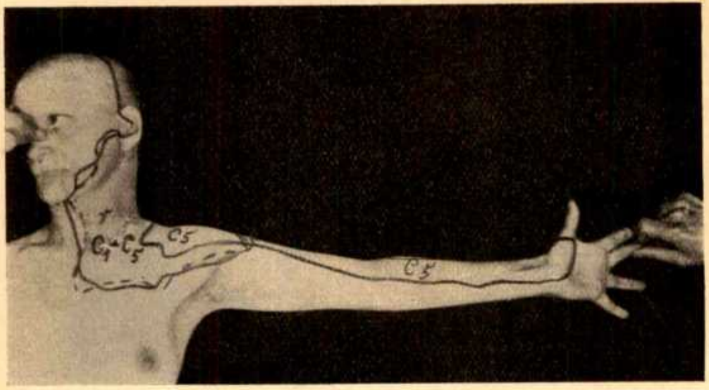


FIG. 66.

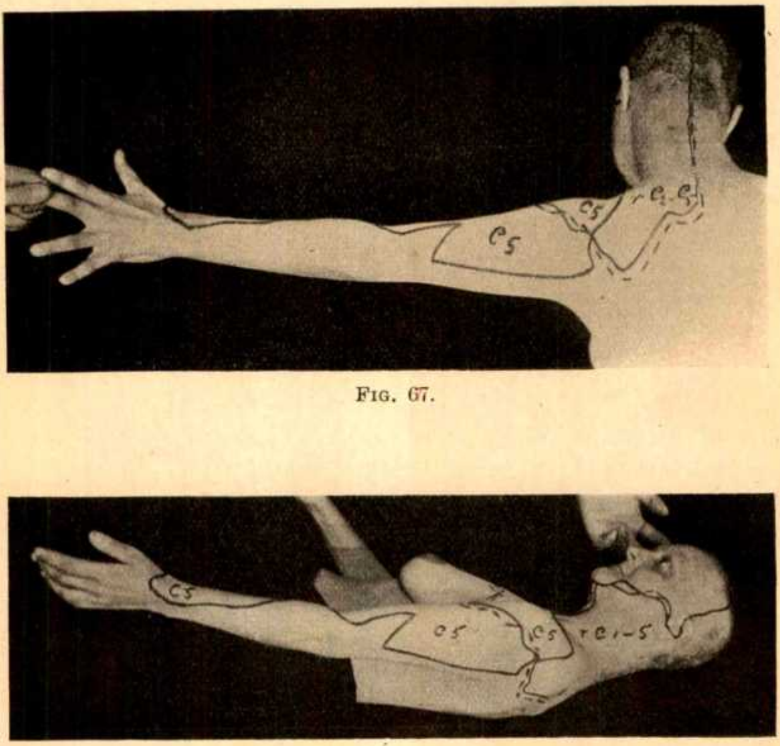


FIG. 67.

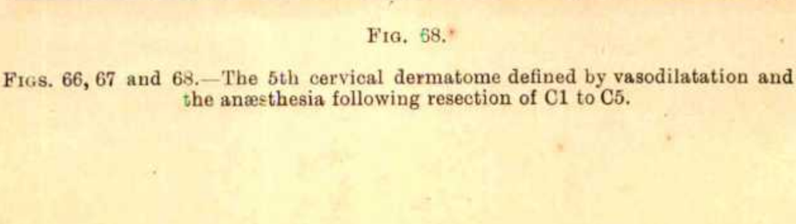


FIG. 68.

FIGS. 66, 67 and 68.—The 5th cervical dermatome defined by vasodilatation and the anæsthesia following resection of C1 to C5.

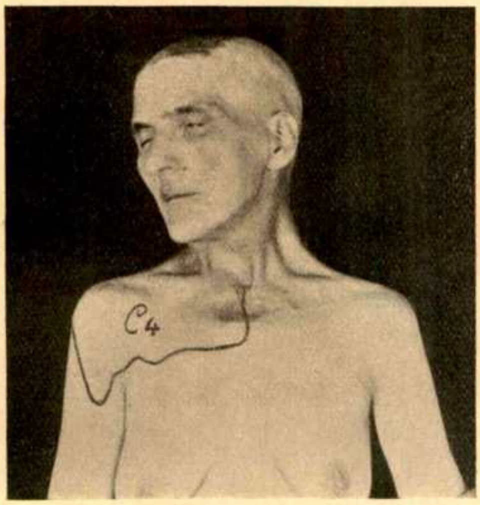


FIG. 69.

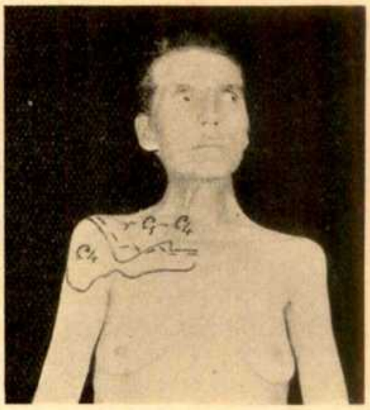


FIG. 70.

FIG. 69.—The inferior border of 4th cervical dermatome, defined by vasodilatation.

FIG. 70.—The inferior border of 4th cervical dermatome, defined by vasodilatation, and the inferior border of the anæsthesia following resection of C1 to C4. This figure demonstrates the large overlap of the 4th cervical dermatome on the adjacent dermatomes.

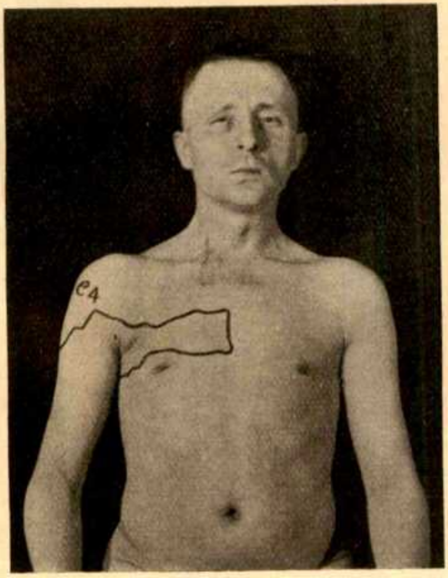


FIG. 71.

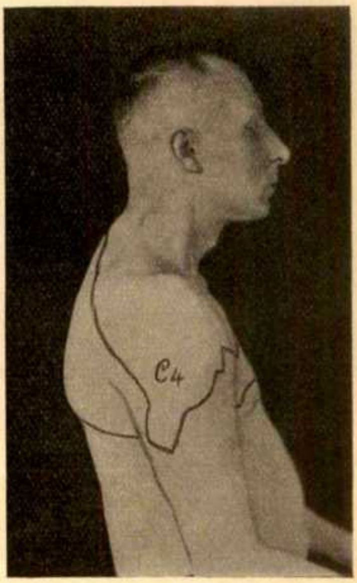


FIG. 72.

FIGS. 71 and 72.—The superior border of the anæsthesia, following resection of C5 to Th4. It demonstrates the inferior border of 4th cervical dermatome.

*The second cervical dermatome* occupies the occiput and the submental region, as may be seen in a case in which all cervical roots except the second were divided (figs. 82, 83). The anæsthesia involves the ear and sends a triangular projection towards the temporal region. But there exist considerable individual variations in the extent of the second cervical dermatome, for in a case in which the same roots were resected and the second cervical root alone was left intact, the ear is partially included in the anæsthesia (fig. 84); on the other hand the loss of

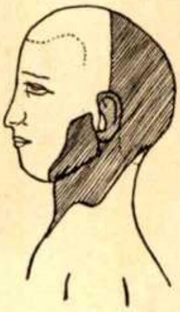


FIG. 73.—The inferior border of the anæsthesia following resection of C2 to C3 (according to Cushing). It demonstrates the superior border of the 4th cervical dermatome.

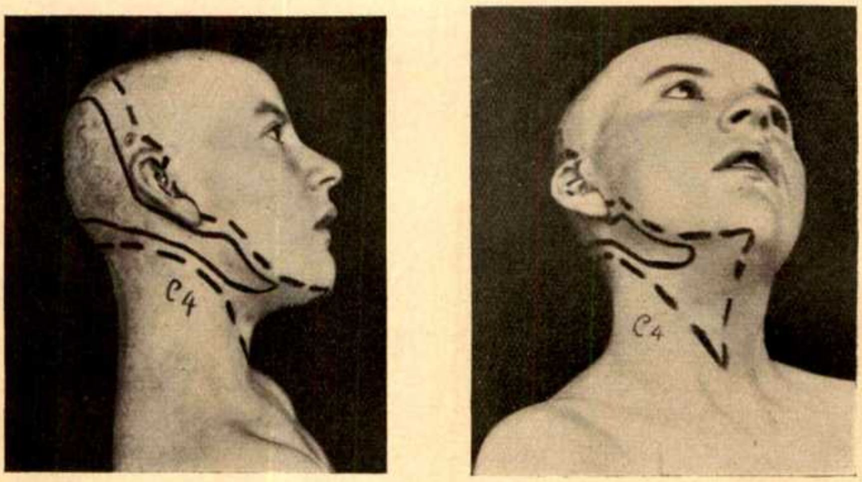


FIG. 74. FIG. 75.

FIGS. 74 and 75.—The anæsthesia following resection of C2 and C3. The inferior border of the anæsthesia indicates the superior border of 4th cervical dermatome. Note the much larger extent of the analgesia – – – than of the tactile anæsthesia ———.

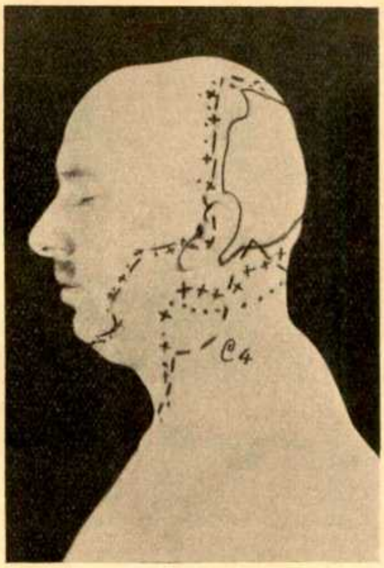


FIG. 76.

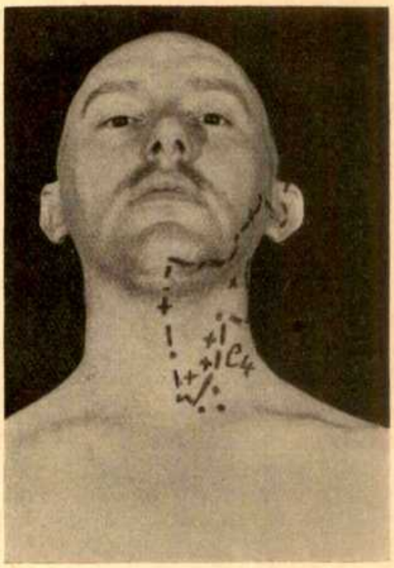


FIG. 77.

FIGS. 76 and 77.—The anæsthesia following resection of C2 and C3. The inferior border indicates the superior border of the 4th cervical dermatome. Note the small extent of tactile anæsthesia ———, the much larger extent of the analgesia – – –, and of thermanæsthesia +. +. +.

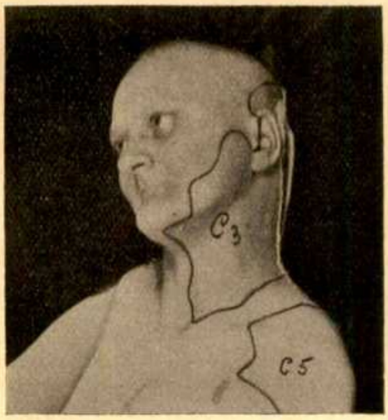


FIG. 78.

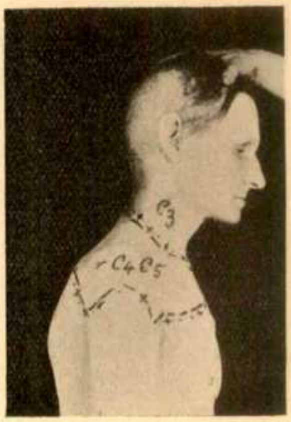


FIG. 79.

FIG. 78.—The 3rd cervical dermatome defined by vasodilatation.

FIG. 79.—The inferior border of the 3rd cervical dermatome defined by the superior border of the sensory loss following resection of C4 and C5. Note the complete absence of tactile anæsthesia in this case.

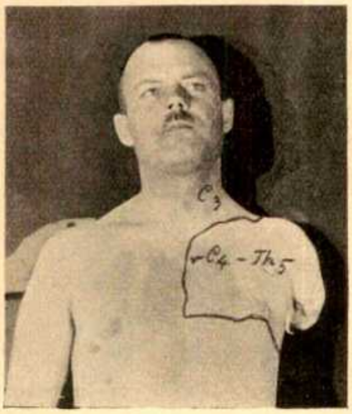


FIG. 80.

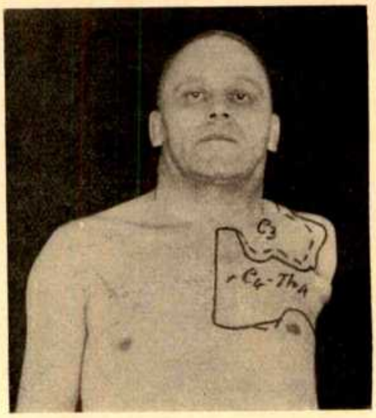


FIG. 81.

FIG. 80.—The inferior border of the 3rd cervical dermatome defined by the superior border of the anæsthesia following resection of C4 to Th5.

FIG. 81.—The inferior border of the 3rd cervical dermatome defined by the superior border of the anæsthesia following resection of C4 to Th4. Note the large extent of the 3rd cervical dermatome upon the thorax.

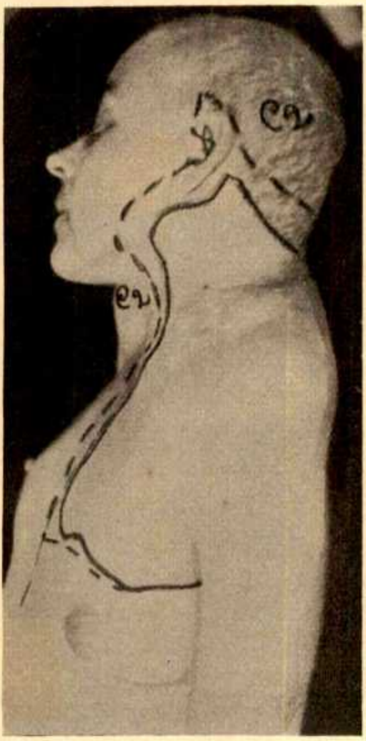


FIG. 82.

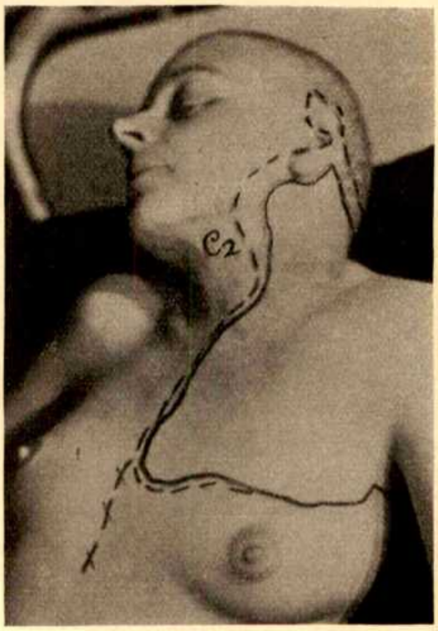


FIG. 83.

FIGS. 82 and 83.—The 2nd cervical dermatome defined by the superior border of the anæsthesia following resection of all the cervical roots except the second.

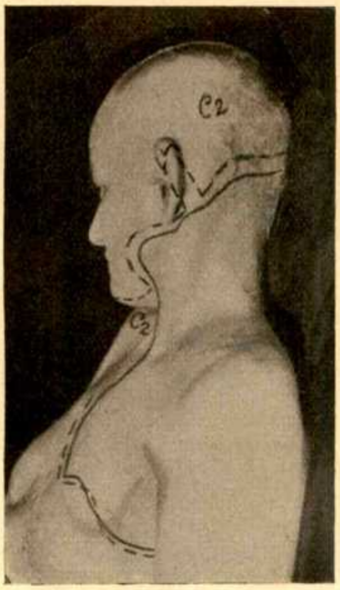


FIG. 84.

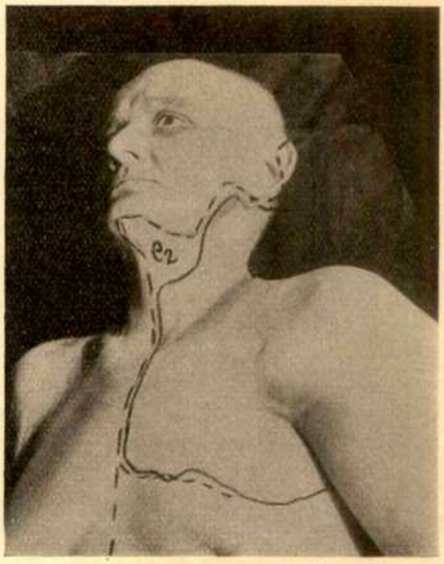


FIG. 85.

FIGS. 84 and 85.—The 2nd cervical dermatome defined by the superior border of the anæsthesia following resection of all the cervical roots except the second.

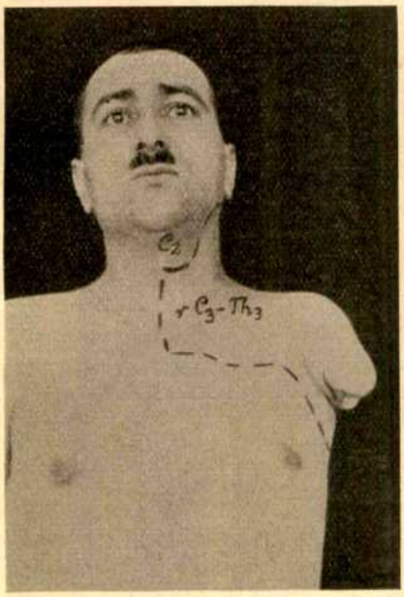


FIG. 86.

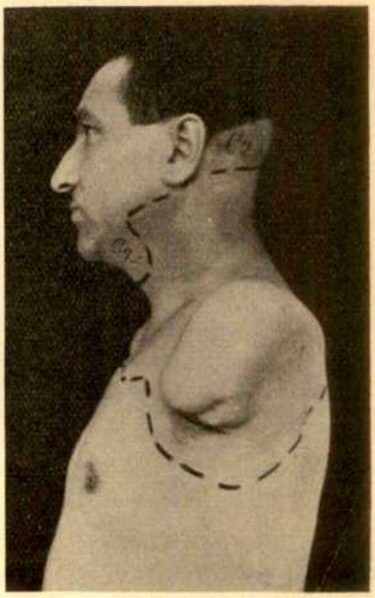


FIG. 87.

FIGS. 86 and 87.—The 2nd cervical dermatome defined by the superior border of the anæsthesia following resection of all the cervical roots except the second.

sensation, at least as far as pain sensibility was concerned, extended into the submental region (fig. 85). In a third case of resection of all cervical roots except the second, the second cervical dermatome occupied the occiput, a large area on the neck and the submental region (figs. 86, 87). The distribution of the anæsthesia was similar in a further case in which the third, fourth, fifth and sixth cervical roots were divided; here the second cervical dermatome extends from the occiput

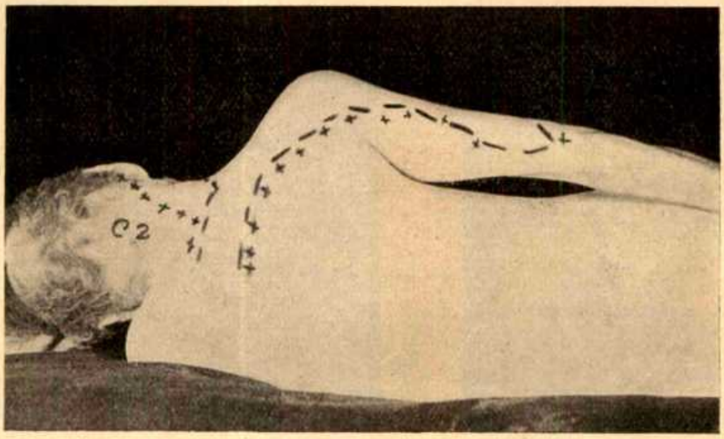


FIG. 88.

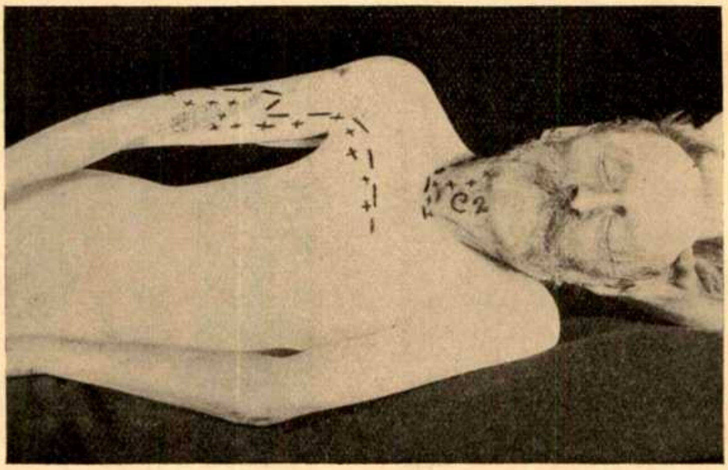


FIG. 89.

FIGS. 88 and 89.—The 2nd cervical dermatome defined by the superior border of the anæsthesia following resection of C3, C4, C5 and C6.

far down on the neck and occupies a large area on its anterior surface (figs. 88, 89).

The oral border of the second cervical dermatome is represented by the border of anæsthesia following resection of the fifth cranial nerve (fig. 90). In the majority of my cases the line separating these two areas runs down from the vertex anteriorly to the ear, but the tragus is not included in the anæsthesia, and I have seldom found the helix anæsthetic. But the observations of other investigators indicate that individual variations exist. Fig. 91 shows the area of anæsthesia following section of the trigeminal root according to Cushing; the tragus is included within it.

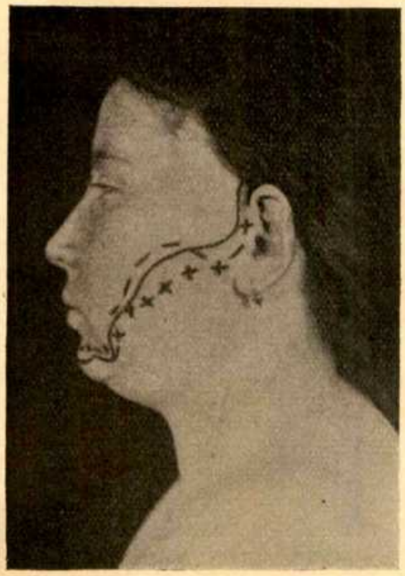


FIG. 90.

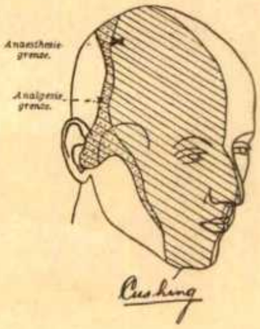


FIG. 91.

FIG. 90.—The superior border of the 2nd cervical dermatome defined by the caudal border of the anæsthesia following resection of the 5th cranial nerve.

FIG. 91.—The tactile anæsthesia and analgesia following division of the trigeminal root, according to Cushing.

The caudal border of the dermatomes corresponding to the cranial nerves, if such an expression be allowed, is represented, according to my experience, by a very typical line. I have been able to determine this in twelve cases in which I resected all the upper cervical roots (figs. 92, 93). In all these cases the anæsthesia included the ear, but the external meatus and the skin around it were not anæsthetic. The individual variations are slight. I believe that it is not correct to say that this border is the caudal limit of the skin supply of the fifth cranial nerve, for we must bear in mind that the seventh, ninth and tenth cranial nerves participate to some degree in the supply of the ear.

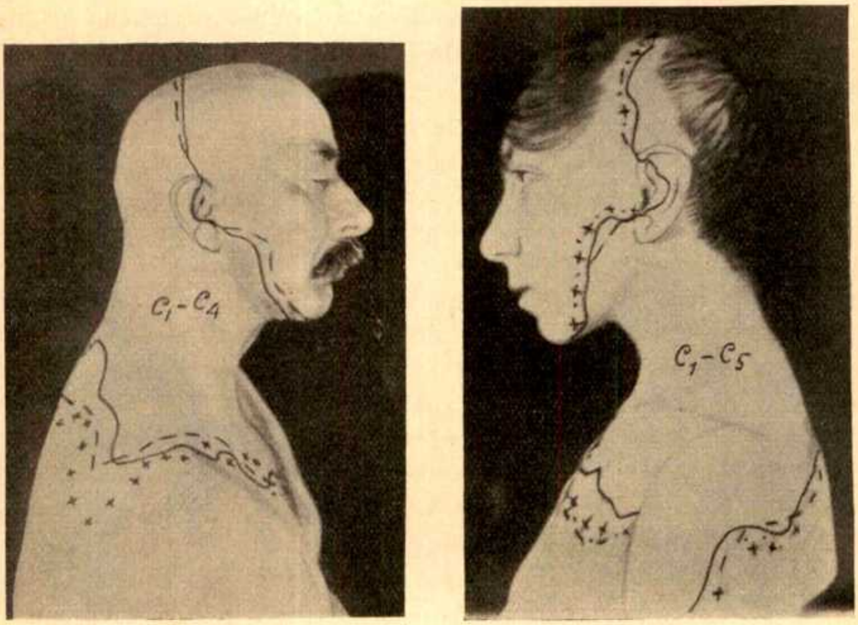


FIG. 92. FIG. 93.

FIGS. 92 and 93.—The superior border of the anæsthesia following resection of all the cervical roots; it indicates the caudal border of the cranial nerve supply to the skin.

### CONCLUSIONS.

From the material at my disposal several conclusions seem to me permissible.

(1) The dermatomes of man overlap to the same large degree as do those of the monkey. I never have found that resection of one single root in man was followed by loss of sensibility; at least by the usual clinical methods of examining sensibility no defect could be detected. When a single posterior root has been divided it is only by counting carefully the number of pressure and pain spots in the area innervated by that root, and by measuring exactly the threshold of the spots for mechanical or electrical stimuli, that a diminution in the number of root fibres connected with the skin can be demonstrated.

(2) The tactile dermatomes are larger than the pain and the thermal dermatomes. The area of analgesia and thermanæsthesia following resection of a number of contiguous roots is always larger than the area of tactile anæsthesia. Sometimes the resection of two contiguous roots produces analgesia and thermæsthesia, only, but no tactile anæsthesia.

(3) The areas of vasodilatation produced by electrical stimulation of posterior roots are similar to the dermatomes defined by the isolation method, but not identical with them. The former are very similar to the areas of herpetic eruption.

(4) One last word to illustrate the conformity between the dermatomes of man and monkey. A single dermatome is represented not only in the totality of the corresponding root, but in every single filament of the root. When all filaments except one of each of a number of roots are cut, no anæsthesia results, each of the corresponding dermatomes preserves its sensibility. This was demonstrated in animals by several investigators. The same is to be observed in man. I have resected in several cases about two-thirds and even more of each of all the lumbar and sacral roots, leaving intact a small filament only of each root. In these cases the sensibility was preserved.

(5) The difference between the results of experimental physiology in animals and clinical observation in man lies in the far greater difficulties presented by human material. The physiologist can do what he believes to be necessary for his investigation; the activities of the neurologist are limited to procedures which are necessary to help his patient, and he can do no more. This difference explains why the physiology of the nervous system of man lags far behind the experimental physiology of animals, and needs more time to achieve a result, which even when obtained will be a modest one.

The material which I have brought before you is the result of thirty years of neuro-surgery, and at the end I feel that I am at about the same milestone as at the beginning. I realize that all our present knowledge of the dermatomes in man has added little to the foundation which was laid just forty years ago by Henry Head in his doctorial thesis in Cambridge, June 1892.

It has given me much pleasure to be invited to deliver this lecture in memory of Dr. Schorstein, who was an eminent physician on the Staff of the London Hospital, more especially as it gives me the opportunity of paying a tribute to his colleague, Sir Henry Head, whose work on the dermatomes and other subjects has added distinction to English neurology.

# OBSERVATIONS UPON THE FORM AND NATURE OF THE "GRASPING" MOVEMENTS AND "TONIC INNERVATION" SEEN IN CERTAIN CASES OF LESION OF THE FRONTAL LOBE.

BY F. M. R. WALSHE AND E. GRAEME ROBERTSON.

(*From the National Hospital, Queen Square, London.*)

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## INTRODUCTION.

THE group of motor disorders that have been described under the various titles of "tonic innervation," "the grasp reflex," "forced grasping and groping," and under comparable descriptive names by writers in other languages, has been the subject of growing interest within recent years.

In each succeeding description they have assumed more complex features, until by some writers they have come to be endowed with qualities which conform to no known natural laws. But while the different studies have been as fruitful of nomenclature as of hypotheses, they have not achieved general agreement upon essential clinical details, nor have they removed the great obscurity which still surrounds the origin and nature of the disorders in question.

Therefore, a fresh clinical study needs no apology.

While it is not proposed to preface it with yet another review of the relevant literature, a brief summary of the recorded facts of observation will serve to indicate the present state of opinion.

In 1914, Wilson and Walshe [17] described a disorder of movement which they called " tonic innervation." It was observed in the paretic arms of patients with frontal lobe lesion associated with hemiparesis. They found that voluntary flexion and extension of the arm and voluntary grasping were followed by considerable delay in relaxation, and in the case of the hand by an inability to release the grasp of any object held in it. Any attempt by patient or by observer to extract the object led at once to greatly increased force of grasp, a tonic contraction of the muscles concerned which persisted until the attempt to extract the object ceased. When the grasp was not forced in this way, the hand frequently opened without difficulty. No reflex factor in the initiation of this tonic innervation was detected.

In 1923, Riddoch and Brain [10], in describing a comparable state of affairs, suggested that a palmar reflex might be in question, the stimulus being a touch on the palm.

Almost at the same time, Schuster [12], and later Schuster and Pinéas [13, 14], published lengthy studies of these grasping and tonic phenomena, which they also noted in the paretic arms of patients with frontal lobe lesions. They found as follows :—

(1) That the hand closed over and grasped any object laid upon the open palm.

(2) That the hand grasped involuntarily and even against the patient's will at any object, such as the examiner's finger, that touched the palmar aspect of the hand or digits, and that the hand and arm turned actively towards the stimulating object, following this as though it were a magnet.

(3) That the hand involuntarily grasped at any object brought near it, even before contact with the palm was made.

(4) That the hand involuntarily grasped at and followed an object that had been withdrawn from its grasp or from its neighbourhood.

(5) That any attempt to extricate an object from the grasping hand led to a strong tonic grasp.

(6) That when the clenched hand was empty—whether actively or passively closed—voluntary relaxation was easy and no tonic grasp ensued.

Schuster concluded that the grasping movements (" Zwangsgreifen und Nachgreifen ") were involuntary and not within the patient's control, and that the exciting stimulus was the contact of some object with the palm or fingers. He explained the tonic grasp as a kind of tetanic fusion of individual grasping movements elicited by the rhythmically repeated tactile stimuli delivered by the object contained within the hand.

In 1927, Adie and Critchley [1], in a small series of clinically and pathologically similar cases, confirmed all these findings and amplified them as follows: (1) The grasping movement of the fingers ensues upon any moving contact with the palm, the stimulus being most effective when applied over the metacarpo-phalangeal joints. A touch on thumb or index in this situation evokes a "crab's claw reflex" in which these digits close upon the stimulating object.

(2) The hand, arm and even the trunk are actively turned towards the stimulating object when the palm is touched, and when this is done repeatedly the limb may be drawn in any direction as though by a magnet, and this even when the patient's eyes are closed.

(3) All these complicated movements occur without the knowledge of the patient, who remains unconscious of them, although—paradoxically enough—he is said to be annoyed by them.

(4) Tonic persistence of the grasp ensues when an attempt is made to pull away any object contained in the hand.

(5) Voluntary clenching of the empty hand evokes no tonic grasp and relaxation in these circumstances is rapid and easy.

(6) The patients in whom these movements are seen are psychically normal at the time of their occurrence.

Adie and Critchley believe with Schuster that they are dealing with a reflex response to sensory (tactile) stimulation of the hand, but in respect of the grasping that occurs before the hand has been touched they express no more precise conclusion than that this provides evidence of phenomena "on a still higher plane."

Such, then, is the present state of knowledge, but the attempt to construct from it a complete, consistent and credible picture of the events described is difficult, if not impossible, because so much is left unaccounted for, and because the role attributed to sensory stimulation of the hand is clearly not in harmony with the recorded facts.

For example, we see (1) that tactile stimulation of the hand is not necessary for the occurrence of grasping movements, for the hand grasps an object that is merely seen, but not felt. It moves towards the approaching and follows the retreating hand of the examiner. Such movements through space can occur only in response to stimulation of a distance receptor, such as the eye.

Nevertheless, Adie and Critchley, though not Schuster, state that these excursions of the limb do occur when the patient's eyes are shut and he is deprived of vision, and that if the hand be repeatedly touched in these circumstances it follows the stimulating object as though this were a magnet. Now a tactile stimulus is effective only at the moment of contact. Before the examiner's finger-tip is actually felt, and after it has left the patient's palm, no stimulus is acting. No one can anticipate the direction from which the stimulating finger is approaching, nor determine the direction in which it is retreating, unless it is seen throughout the whole procedure.

That the hand of the patient without vision should advance to and follow the stimulating finger is not possible. Equally unacceptable is the statement that these very complex movements, even when directed by vision, may be made by a psychically normal individual without his being aware of the fact. More in accord with reason is the statement of Schuster that his patients make these grasping movements in response to an urge to do so, but whether this be the case or not, it seems certain that they must know what is happening.

We see also (2) that tactile stimulation of the hand is effective only under certain special conditions, namely, that the stimulating object must be a foreign body presented in a certain way. For when the patient closes his empty hand, no "forced grasping" ensues and he can open his hand easily. Yet his own finger-tips, when he encloses them in his fist, deliver a sensory stimulus to the palm differing in no single physiological respect from that delivered by the examiner's finger-tips. This observation at once takes the grasping movements out of the category of true reflex movements.

(3) Schuster regards the tonic grasp as the fusion of a series of separate grasping movements ("eine ununterbrochene Aufeinanderfolge einzelner Greifbewegungen") evoked by repeated tactile stimulation from the object contained in the hand. We cannot regard this conclusion as resting upon a sound physiological basis. An object at rest in the hand rapidly ceases to be a potent source of tactile stimuli, and it is difficult to regard the tonic grasp as a kind of tetanus of phasic contractions. It has the characters of a true tonic reflex, a mode of reaction which exteroceptive, tactile stimuli are not adequate to elicit. The possibility that a proprioceptive stimulus may be in question has not been raised by any of the students of this phenomenon, though it leaps to the eye.

(4) Finally, some importance attaches to the psychical condition of the patients in whom these movements occur. Adie and Critchley make

the general statement that this is normal, but reference to the case details given in their paper shows that two of their three patients were grossly abnormal in this respect, while of the third nothing is said as to his condition in this respect at the relevant period of his history. All Schuster's patients were mentally reduced, and when we recall that all cases of the kind have lesions of the frontal lobe—either tumours or softenings within the territory of the anterior cerebral artery—it is not surprising that in fact all show some disorder of volitional control and activity.

Therefore, a survey of the clinical information available indicates that the factors responsible for "forced grasping and groping" still remain to be elucidated, and that some of the recorded facts of observation are themselves suspect.

## CHAPTER I.—CLINICAL OBSERVATIONS.

If there be any reflex factors in the phenomena we are considering, their presence and characters can be revealed only by a methodical search for the essential components of a true reflex reaction; namely, a specific mode of stimulus, a definite and constant receptive field, and a uniform, co-ordinated motor response. These are the elements of the reflex reaction of the segmental nervous system, with which the researches of Sherrington have made us familiar.

Further, in the event of such a factor being found, we have still to determine whether it includes the whole range of observed movement, or whether it is but a fraction of a larger movement-complex not all of which is reflex in nature.

A preliminary survey of a case presenting the phenomena that we are considering certainly gives the impression that the grasping *movements* with their striking range and delicacy of adaptation from moment to moment, and their apparent independence of sensory stimuli from any single receptive field, are scarcely likely to be true reflexes. On the other hand, the *tonic innervation* of muscles shows a uniformity of behaviour and a dependence upon a single mode of sensory stimulation which suggest strongly that here we are indeed dealing with a reflex reaction of the fixed, inborn variety.

Our own study of a series of eight cases has in fact led us to the conclusion that phenomena of two categories are to be observed, of widely different physiological rank, the one volitional and the other a true reflex reaction.

The clinical material upon which this conclusion is based may now be described in detail. Not every observed case is reported in full, but such as illustrate the initial evolution of grasping movements and of tonic innervation, their full development and their progressive extinction or dissolution. The cases not reported here are but additional examples and differ in no essential respects from those described.

*I.—Cases illustrating the onset and evolution of grasping and of tonic innervation.*

*Case* 1.—H. T., a man, aged 59. (National Hospital, 1933, Dr. F. M. R. Walshe.)

*History.*—For six months he has been subject to "attacks" in which a peculiar feeling came over him, he flushed and looked vacant, no loss of consciousness. On coming to he said that a sharp pain had darted down the right side of his body into his leg, that the right limbs had stiffened, but had not moved. For the same period he complained of headaches.

For past three months he had noticed that at times he could not "let go" with the right hand when he was holding something in it.

For some months, his wife said, he had been irritable, forgetful and altered in disposition.

A week ago after an "attack" the right leg began to drag.

First examination (January 7, 1933). Fully conscious and co-operative. An unreliable witness, rather fatuous in manner. Speech normal.

Optic discs: slight haziness of upper edges. A small hæmorrhage in left fundus. Quadrantic defect of right visual fields, right and left eyes.

Pupils and ocular movements normal. No facial asymmetry. Tongue protruded straight. Corneal reflexes normal.

Motor system: A slight right hemiparesis, leg most affected, face unaffected. Left limbs normal.

Sensory system: Slight impairment of tactile acuity, of localization, of two point discrimination and of appreciation of size and form in right hand. Painful and thermal sensibility normal. Comparable sensory impairment in right foot.

Reflexes: Tendon-jerks brisker right than left. Transient clonus right ankle.

Abdominal reflexes diminished on right. Right plantar extensor, left flexor.

*Right limbs.*—Passive movement of the right arm evokes a tonic resistance in biceps and the elbow flexors, a resistance persisting throughout the whole range of movement and until the arm is released. The limb is slightly tremulous in use and finger movements are a little clumsy. No trace of delayed relaxation in voluntary movements.

*Grasping movements.*—When the observer's fingers are slipped into the patient's right palm between his thumb and index, the patient's fingers close gently on them and hold in a gentle clasp. At request the patient can open his hand freely provided that the fingers in his clasp remain quite still.

When the examiner's index finger is gently introduced between the patient's thumb and index so as to stroke the fold of skin between them, it is met by a gently closing movement of these digits. Unless the skin is touched there is no movement, and there is no movement of the patient's arm through space to meet or follow the examiner's finger.

The patient can prevent the occurrence of the grasping movements described, when asked to do so.

When the examiner's finger is introduced into the patient's palm from the ulnar side, there is usually no grasping, but vigorous rubbing of the palm sometimes evokes a grasping movement of the fingers.

When the patient's hand is turned palm upwards and supported on the palm of one of the examiner's hands, it can be touched with cotton-wool, stroked, pressed and pricked with a pin without any trace of grasping response.

*Tonic innervation.*—None of the procedures described above evoke any trace of tonic grasp. But this is constantly produced when the examiner pulls his fingers out of the patient's clasp, especially if this is done so as also to pull on the arm. This tonic grasp persists indefinitely and until the pull is released, when he can open his hand easily.

The same tonic response is elicited by placing the handle of a wooden stethoscope transversely within the crook formed by the patient's semi-flexed fingers and giving a sharp pull so as to stretch the flexors of the fingers. The patient cannot prevent the development of this tonic contraction of his finger flexors, and when asked to let go, makes a series of efforts. At first the fingers open out at the metacarpo-phalangeal joints, the interphalangeal joints remaining flexed. Further efforts finally allow these to open after some seconds delay.

He can open his empty fist without any delay or difficulty, and he can also open his grasp with equal ease when it contains the wooden handle of the stethoscope, provided that the latter lies free in his hand.

Occasionally, as the handle drops downwards its bell-shaped end strikes against the side of the patient's thumb and this may elicit a short closing movement of thumb and index. But if a plain straight object be used this does not occur.

Subsequent examinations: During the week after admission to hospital, the headaches and the "attacks" ceased, and all the phenomena described above were unobtainable. Sometimes manipulation of the hand led to the appearance of tonic contraction of the flexors of the fingers to stretch, but no grasping *movements* were obtainable.

He was then given $\frac{1}{100}$ gr. of hyoscine hydrobromide hypodermically. An hour later examination gave the following results. He was a little somnolent and fatuous when aroused, but could be made to co-operate easily.

The right hemiparesis was a little more marked than previously. To stroking and touching of the palm and of the skin between thumb and index there were quick grasping movements, but no tonic innervation. Uncertain grasping to stroking of ulnar side of palm. Sensory testing of the upturned palm as described above gave no trace of grasping movements.

He could open the empty hand, or the hand containing a wooden rod easily.

The flexors of the elbow showed marked tonic resistance to stretching. Tonic innervation to stretching of the finger flexors was well marked and forceful and well sustained.

The patient could prevent the occurrence of grasping movements, but had no vestige of control over the development of tonic innervation of the finger flexors to stretching.

*Summary.*—A case of right hemiparesis, the leg being most affected, with sensory changes of cortical type and an incomplete right homonymous hemianopia. The motor symptoms suggest the presence of a frontal lobe lesion near the mid-line and vertex. The sensory and visual signs suggest the presence of other lesions. The ophthalmoscopic appearances are compatible with an early papilloedema. At the time of writing it seems probable that multiple tumours are present. Grasping movements and tonic innervation are developing and can be released when absent by the administration of hyoscine. Tonic innervation seems to be the first of these phenomena to appear. It is elicited only by stretch of the muscles concerned. It is not within the patient's control. Grasping movements are obtained to certain specialized tactile stimuli applied to part of the hand, but not to other tactile stimuli of identical physiological quality. These movements can be prevented by the patient.

*Case* 2.—W. C., a man, aged 55. (University College Hospital, 1933, Dr. F. M. R. Walshe.)

*History.*—For six weeks he has been subject to frequent attacks, consisting of stiffness of the right limbs, turning of the head to the right and then clonic movements of the right arm and leg. The attack begins in the leg, which is more severely affected than the arm or face. No loss of consciousness, nor of speech during attack. Headaches since first attack, and progressive weakness of right limbs, especially of the leg.

Examination: January 13, 1933.—Fully conscious and co-operative, but euphoric and a bad witness. Memory bad. Occasionally at a loss for a word.

Optic discs normal. Visual fields normal.

Slight right hemiparesis, the leg being most affected, the face least. No sensory loss. Tendon-jerks brisker right than left. Right abdominal reflexes diminished. Right plantar doubtful, left flexor.

*Right arm.*—Very slight weakness, but no appreciable hypertonus. Finger movements a little clumsy. Passive movement of the arm is unresisted, but quick passive extension of the hand and fingers evokes a distinct tonic contraction in the flexors.

Grasping. When the examiner's index and middle fingers are slipped into the right palm between thumb and index, the patient's thumb and fingers make a quick grasping movement and hold the examiner's fingers in a gentle clasp. When this procedure is repeated, but the examiner slips his fingers into the palm from the ulnar side of the patient's hand, there is no grasping movement.

If the examiner's index finger repeatedly strokes the fold of skin between the thumb and index of the patient's right hand ; each contact evokes a grasping movement of the patient's thumb and index.

When the patient is told to keep his fingers still under these conditions he can do so without difficulty, but when his attention is distracted the grasping movements resume.

Unless contact is made with the patient's hand there is no grasping, and there is no movement of the hand and arm through space to meet the examiner's hand.

He can open his empty fist quickly and without effort, and if a fountain-pen be placed in his grasp he can open his hand and drop it without delay or difficulty.

When his hand is turned palm up and supported on the examiner's, sensory testing—cotton-wool, stroking and pressure—evokes no trace of grasping.

*Tonic innervation.*—None of the procedures named above evokes a tonic grasp, but if the attempt is made to pull the fingers or any other object contained in the patient's grasp away—especially if the pull is away from the patient—a tonic contraction of the finger flexors at once ensues and persists until the pull is released, when he can open his hand without difficulty.

If the examiner's index finger or a wooden rod is placed in the curve of the semi-flexed fingers of the patient's hand, and then pulled brusquely so as to stretch the flexors, tonic contraction of these muscles ensues and the patient can be pulled into a sitting position in the bed. He cannot open his fingers until the pull is released.

There was no trace of tonic innervation in the leg.

*Summary.*—A case presenting the clinical signs of a left frontal neoplasm. Grasping movements of the fingers are elicited by certain forms of tactile stimulation of the hand, but not by others. No tonic innervation is elicited in this way. The patient can readily prevent the occurrence of grasping, and he can readily open the empty hand, or the hand containing an object, provided that the latter is in no way interfered with so as to stretch the finger flexors.

Tonic innervation is elicited by stretch of the finger flexors, and by no other mode of stimulus. It is not within the patient's control, *II.—Cases illustrating fully developed grasping and tonic innervation.*

*Case* 3.—Davis, A., a tailor's cutter, aged 43. (National Hospital, 1931, Dr. Hinds Howell.)

*History.*—Eighteen months, headache, depression and irritability. Four weeks, apathetic and unable to speak. One week, progressive stupor with incontinence of urine and fæces. Lay motionless in bed staring vacantly before him.

*Condition on examination.*—Conscious and well oriented. No spontaneity of speech or action, lies motionless and speechless in bed. Occasionally rubs his nose with his left hand. Can answer simple questions, but cannot give any account of himslf. Attention can be aroused, but wanders easily. Passes urine and fæces in bed. No aphasia or apraxia.

Optic discs, bilateral papillœdema. Visual fields normal to rough test. Severe left hemiplegia, with a very slight right hemiparesis. All tendon-jerks brisk, abdominal reflexes lost on both sides. Plantar response extensor on both sides. No evidence of sensory loss.

The left limbs retain a trace of feeble voluntary movement.

*Right arm and hand.*—(1) The right arm lies on the bed-cover, and when the examiner's right hand approaches it within a few inches, the patient's hand slowly moves to it and encloses it in a gentle clasp. When the patient's eyes are covered this movement does not occur. When his hand meets the examiner's he grasps it entire in slow but normal fashion, moving his hand about until he has secured a comfortable grasp. If one of the examiner's fingers eludes his grasp, he opens his hand normally and fumbles about until he has captured and included it in his grasp. He maintains this grasp in an irregularly waxing and waning fashion, but does not tighten firmly on it. In these circumstances, he can release it readily on demand.

(2) If the examiner's hand is now pulled away, especially if in such a way as to extend the patient's arm and digits, the patient's grasp at once tightens and becomes strong. It is maintained as long as the pull is kept up, and the patient cannot relax voluntarily or to order.

(3) The patient's hand is cupped and supported on the examiner's hand, so that no passive extension of his fingers is possible. Cotton-wool touch, local pressure, pin-prick on the patient's palm evoked no trace of grasping movement. Vigorous rubbing of the palm is also ineffective.

(4) A tonic grasp is immediately provoked by placing the examiner's index finger, or the handle of a wooden stethoscope, at the base of the half-flexed fingers of the patient's hand, and pushing it into the crook formed by the fingers so as to stretch (extend) them. As long as a pull is kept up the tonic grasp is maintained and cannot be voluntarily relaxed.

A tube of very hot water employed in this way evokes a grasp, which is quickly relaxed, the patient rubbing his burning fingers together.

Similar findings were obtained at a subsequent examination.

*Post-mortem.*—An astrocytoma involving the genu of the corpus callosum and invading both frontal lobes.

*Summary.*—A case of bilateral frontal lobe lesion.

The hemiparetic right hand and arm deliberately reached to the examiner's hand when this approached his, within his sight, and as deliberately secured a comfortable grasp of it. When the procedure was so arranged as not to awaken the notion of grasping in the patient's mind, various forms of tactile stimulation of the hand failed to evoke grasping. On the other hand, stretching of the finger flexors invariably elicited tonic grasping which was maintained as long as the stretch was kept up.

### III.—*Cases illustrating progressive dissolution of grasping phenomena and tonic innervation. Catatonia.*

*Case* 4.—H. B., a man aged 69 (National Hospital, 1932, Dr. W. J. Adie.)

*History.*—Headaches for eighteen months, progressive loss of energy, and apathy for fifteen months, progressive right hemiparesis, confusion, disorientation, drowsiness and double incontinence for seven weeks.

*First examination.*—Stuporose, easily roused, but readily relapsing into stupor. Optic discs show myopic changes, but no papillœdema. Appears to have useful vision and can fix for a minute or so when aroused and spoken to. Will occasionally answer simple questions slowly. No aphasia, no apraxia of left hand. Small but active pupils.

Severe right hemiplegia, with moderate spasticity, but no voluntary power. The right limbs are in characteristic hemiplegic posture. Tendon-jerks increased on both sides, abdominal reflexes all absent. Right plantar response extensor. On the left, the leg flexes, the hallux plantar flexes and the small toes fan.

*Left limbs* show no very definite paresis. He occasionally puts his left hand on his nose or head. At times the resting hand gently clasps the bedclothes, but leaves these during movement without any difficulty. To palpation the muscles of the limb are flaccid.

(1) *Passive movement of the arm.*—If the limb is gripped round the wrist and passively extended, biceps and supinator at once go into tonic contraction and stand up under the skin, revealing their contours. There is marked resistance to stretching throughout the range of extension. If the arm is then flexed, a similar, but less marked, resistance is felt in the extensors.

(2) *Grasping movements.*—The patient lies on his back, gazing upwards with eyes half closed. His hand lies on the bed, and is not within his view. The examiner's hand is then moved slowly towards it. It makes no move until touched on the palm. It then slowly clasps the examiner's hand, secures

a comfortable grasp and retains its hold in a waxing and waning grasp, never forceful.

(3) *Tactile stimulation of the palm.*—The patient's left hand is cupped and supported as described above. Cotton-wool touch, pin-prick and local pressure on palm and fingers evoke no grasping movement.

(4) *Tonic innervation.*—The examiner's hand, as it lies within the patient's, is now pulled so as to extend the arm and digits of the patient's limb. A tonic forceful grasp at once develops, and is sustained. The patient's head and back can be pulled off the bed without the grasp relaxing. Brusque orders to him to relax have no effect.

(5) *Left lower limb.*—This lies half flexed and abducted. At times it is slowly extended and again flexed. Passive extension at the knee evokes a strong tonic resistance and the stretched muscles stand out under the skin, as described in the case of the left arm. Stimulation of the sole (stroking movements with finger) evoke a slow plantar flexion and bunching of the digits, and a slow resumption of their original position after two or three seconds. At times the small toes fan instead of plantar flexing, and the limb flexes.

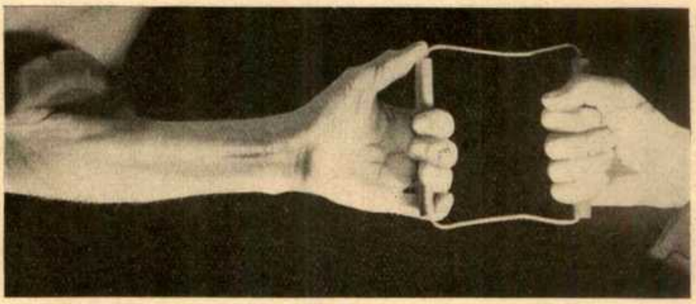

FIG. 1.

*Second examination* (November 29, 1932).—Apparently asleep, and with Cheyne-Stokes' respiration. Rouses somewhat during examination, when respiration may become continuous.

During apnœa. The left arm lies flaccid and shows no trace of tonic resistance to passive movement. The left leg is similarly flaccid. On the other hand, the spastic right limbs retain their habitual degree of hypertonus.

*During respiration* the tonic resistance of the left limbs on passive movement rapidly returns. Also the grasping movements of the left hand described above, which were completely in abeyance during apnœa, return.

If when the examiner's hand is clasped by the patient's, a finger of the examiner's hand eludes his grasp, the patient's hand opens again and his fingers fumble until they have enclosed the complete hand in a comfortable grasp. The tonic grasp can be elicited as on the previous examination.

*Third examination* (November 30).—Stuporose and in Cheyne-Stokes' respiration.

*During apnœa* left limbs flaccid and no grasping phenomena or tonic innervation obtainable. Pupils dilate slightly during this phase, and there is also a uniform slight diminution of the tendon-jerks, and plantar stimulation of the left sole evokes dorsiflexion of the hallux.

*During respiration* the left limbs resume their tonic contraction to stretching, and grasping phenomena-movement and tonic grasping reappear. The hand grasps the examiner's hand, but fails to grasp when given tactile stimuli as described under paragraph 4 in the first examination. Also when clasping the examiner's hand, the patient's hand relaxes quickly if the base of the palm or thumb be pricked with a pin. A tonic grasp can be elicited by the procedure described in paragraph 3 above.

Third examination (November 30).—Semi-comatose. Cheyne-Stokes' respiration.

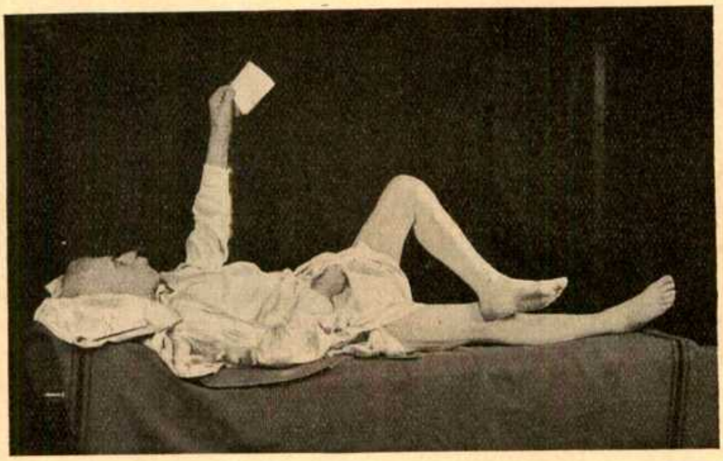

FIG. 2.

*During apnœa* left limbs flaccid, no trace of grasping phenomena. Right limbs retain their customary spasticity. Plantar response from left foot was sometimes plantar flexion and bunching of all toes and sometimes dorsiflexion of the hallux. Biphasic responses were also noticed.

Respiration became continuous during examination. The tonic resistance of left limbs and the grasping phenomena returned. At times when gently grasping the examiner's hand—during this and other examinations—the patient's left hand would actively and easily relinquish this grasp and travel down to his penis when about to micturate, or up to his face to rub his nose.

Fourth examination (December 5).—Semi-comatose, regular respiration. No response to presence of examiner. Left limbs show tonic innervation to stretching. No grasping movements to any mode of stimulation of the hand, but a rod placed in the curve of the semi-flexed fingers and pulled brusquely so as to stretch the finger flexors evokes a tonic contraction of these muscles of moderate intensity. Thus, tonic innervation to stretch is the last remaining component of the grasping phenomena (fig. 1).

During the greater part of the period of observation the patient presented a catatonic condition of the left limbs. These retained for several minutes any posture imposed upon them, as is illustrated in fig. 2.

*Post-mortem* examination a few days after the last clinical examination revealed the presence of two cerebral tumours, one in the upper part of the left temporal lobe, the second in the left frontal lobe, near its mesial aspect and invading the corpus callosum. A large recent hæmorrhage was present in the latter. Histologically the tumours were gliomatous.

*Summary*.—A case of left frontal and temporal lobe tumours, presenting right hemiplegia, very slight left hemiparesis with grasping movements and tonic innervation of the left limbs. Under observation, the former gradually diminished and disappeared, tonic innervation of the flexors of the fingers persisting later. The grasping movements occurred in response to certain special forms of tactile stimulation of the hand, but not to other forms. Tonic innervation of the finger flexors was obtained only in response to stretch of these muscles and not to other forms of stimulus.

*Case* 5.—W. F. S., man aged 49. (National Hospital, 1933, Dr. S. A. K. Wilson.)

*History*.—Six months before admission to hospital had three generalized convulsions with loss of consciousness, within three weeks. Subsequently became progressively apathetic, confused and silent. Could not be got to answer questions. Complained of headache at time of onset. Progressive left hemiparesis, incontinence of urine.

*First examination* (December 19, 1932).—Conscious, motionless and silent. Will give his name slowly on request, but does not answer other questions. He follows the observers with his gaze.

Optic discs normal. Has useful vision. Fields cannot be tested.

Flaccid left hemiplegia, no voluntary movements can be elicited.

There is no definite right hemiparesis. He moves his right hand up to his nose or head, and back again to the bed from time to time, these movements being slow but otherwise normal and well co-ordinated. There is no visible delay in relaxation.

The tendon-jerks are of normal facility in the left limbs, slightly diminished in the right. Abdominal reflexes absent right and left. Plantar responses extensor right and left.

Sensation cannot be tested, but he makes grimaces when pricked on either side.

*Right limbs*.—The right arm lies semi-flexed on the bed. The muscles are very soft to palpation, but when the arm is passively extended at the elbow, biceps and supinator longus go into strong tonic contraction and stand up beneath the skin in strong relief. It requires considerable force to extend the arm fully, the muscles remaining in tonic contraction until the limb is released (fig. 3).

*Grasping movements.*—The patient's hand is held round the wrist in front of him. He gazes fixedly at it. Repeated stroking movements are made with a pencil on the fold of skin between thumb and index. At each contact, these digits make a grasping movement to enclose it. If the process is repeated *without making actual contact with the skin*, the grasping movements occur as before, but cease immediately the patient's eyes are covered.

The hand is now released and the procedure repeated. The results are the same, except that the hand now moves actively towards the pencil before it reaches the interspace between thumb and index. These movements of the hand and arm through space cease at once when the patient's eyes are covered.

The examiner's fingers are now laid upon the patient's palm. His hand at once closes round them and enwraps them in a natural grasp. If the examiner keeps one or more fingers outside the grasp, the patient's fingers extend normally and make movements until they have enclosed the examiner's elusive fingers, and the hand now settles round the examiner's into a natural grasp. This grasp is gentle and remains so until an effort is made to pull the examiner's fingers away.

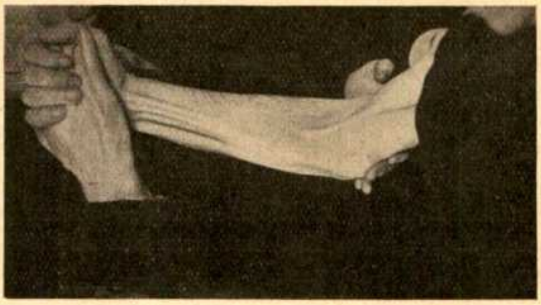

FIG. 3.

*Tonic innervation.*—If the examiner's fingers enclosed within the patient's grasp are pulled slowly away, especially if in such a direction as to stretch the patient's fingers and arm, the arm flexors and finger flexors go at once into strong tonic contraction, so that the patient's head and trunk can be pulled up free of the bed. Brusque orders to the patient to "let go" are without effect, though the patient appears to be trying to open his hand. As soon as the pull is released, the patient's hand opens naturally.

*Tactile stimulation of the hand.*—The patient's hand is laid palm up on the examiner's palm and held. Systematic testing with cotton-wool, pressure and pin-prick evoke no grasping movements and no trace of tonic innervation.

*The empty grasp.*—At times the patient opens his hand voluntarily as it lies free on the bed. There is no delay in doing so. If his hand be closed by the examiner, and he be commanded brusquely to open it, at times he takes no notice, but occasionally he seems to appreciate what is required of him and opens his hand quickly and with ease. There is no tonic innervation in the opening of the empty fist.

*The right leg* lies semi-flexed on the bed. The muscles are flaccid to palpation, but passive extension of the knee or passive movements at the ankle at once evoke strong tonic resistance. The knee flexors stand up under the skin in strong relief, and so remain until the leg is laid down on the bed, when they relax at once and become soft again (fig. 4).

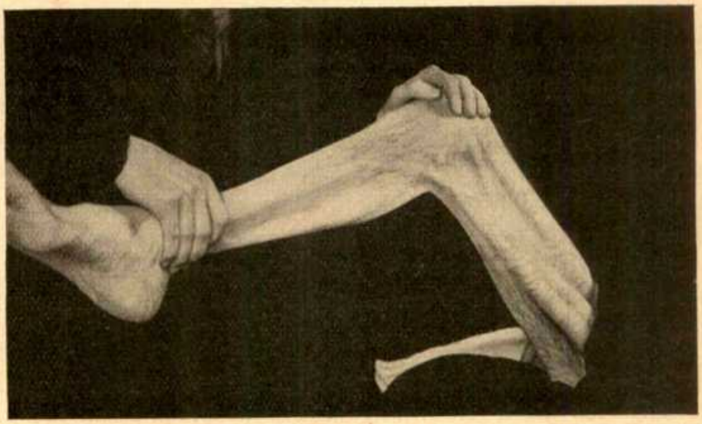

FIG. 4.

Stimulation of the sole by light or heavy stroking or pressure evokes no tonic contraction of plantar flexors, but only a feebly marked extensor response.

Examined during the same evening, the above results were all confirmed, but as soon as the patient fell asleep both grasping to contact and tonic innervation disappeared.

Examination on December 20: State of consciousness as before.

Strong tonic resistance to extension of the elbow or of the knee.

Voluntary movements of arm normal in rate.

Grasping to pencil introduced between finger and thumb as before, both to vision and to touch.

Systematic sensory examination of palm as described above evoked no grasping movements.

Tonic innervation of arm and leg and of grasping muscles to stretch as before.

Examination on January 16, 1933: The patient is now emaciated and feeble, but remains in the same condition of conscious immobility. He is totally irresponsive to questions and orders, and does not fix examiner with his gaze. There are no grasping movements when the palm is stroked, or when the examiner's hand is laid within the patient's.

If the examiner's index finger is placed in the hook of the patient's semi-flexed fingers and brusquely pushed into the digits so as to extend them, they at once go into strong tonic flexion and retain the examiner's finger as long as this is pulled away from the patient.

Examination on January 17, 1933: Patient less apathetic. He fixes examiner with his gaze and at once offers his hand, moving this up off the bed towards the examiner who stands beside the bed. He does not answer questions, or carry out simple orders, such as "Shut your eyes," etc.

He encloses the examiner's hand when this is placed on his in a gentle grasp.

Tonic innervation of arm and of grasping muscles to stretch as before, though not so strong.

Sensory testing of hand with cotton-wool, pressure, &c., evokes no trace of grasping, but immediately afterwards the examiner's hand is placed on the patient's and is again enclosed in a grasp. If a finger eludes the grasp, the fingers open and feel about for the missing finger until it is found, when it is enclosed in a natural grasp.

The patient died on January 26, 1933. Post-mortem examination revealed the presence of a large meningioma of the right frontal region, surrounded except at its point of attachment by a thin shell of frontal lobe. The lobe was greatly expanded by the tumour and extended across the mid-line, compressing the opposite frontal lobe.

*Summary*.—A frontal tumour producing severe hemiplegia on the opposite side with slight hemiparesis on the side of the lesion. The hand and arm on this side displayed grasping movements to certain tactile stimuli applied to the hand, and occasionally the patient offered his hand to the examiner directly he caught sight of him. Tonic innervation was present and could be elicited by stretch alone. It survived after grasping movements had ceased to occur.

*Case* 6.—F. I., a woman, aged 61. (National Hospital, 1931, Dr. Gordon Holmes.)

History: Three months before admission to hospital she suddenly became unable to express herself clearly or to write a coherent letter. She became progressively more silent and apathetic, and within a week was doubly incontinent, confused and unable to construct even a simple sentence She allowed food put into her mouth to remain there unchewed and unswallowed.

On admission she was emaciated, motionless, except for following moving persons with her gaze, and unable to answer questions. She exhibited marked catatonia, her limbs retaining postures passively imposed upon them for a minute or longer. She was incontinent of urine and fæces.

Examination revealed bilateral papillœdema, tonic resistance to passive movement of all four limbs, tendon-jerks of normal facility and equal on the two sides. The abdominal reflexes were present bilaterally, the plantar responses bilaterally flexor.

Her mental state was such that no co-operation with the examiner was possible. She died within a week of admission to hospital and autopsy revealed a small glioma in the left parietal lobe, and a second one on the mesial aspect of the right frontal lobe invading the corpus callosum.

*Grasping movements.*—Touching and stroking of the palmar aspect of hand and fingers elicited no trace of grasping movement. Deep pressure and pin-prick evoked no response of any kind.

*Tonic innervation.*—The patient's hand (right or left) is turned palm up, and the slightly flexed digits are brusquely pressed downwards, i.e., are extended. At once they flex round the examiner's pressing finger and grasp this firmly and for as long as extension (i.e., stretching of the flexors) is kept up. If the examiner now pulls his finger away from the patient so as to extend both arm and digits, this tonic grasp increases in force.

If the patient's hand is fully flexed at the wrist before this procedure is adopted—that is, if the flexors of the fingers are made as lax as possible—then extending the fingers in the manner described elicits either no response or a feeble one.

If now the patient's hand be fully extended at the wrist, then pushing down the fingers (that is, still further stretching the flexors of the digits) evokes a strong tonic flexion round the examiner's pressing index finger.

The legs present the same tonic resistance to passive movement as the arm, but no abnormal response is obtained from the toes by any mode of stimulation of the sole.

*Summary.*—A case illustrating the last stage in the dissolution of the grasping and tonic phenomena, the former having completely disappeared—if we may assume that they were at one time present.

## CHAPTER II.—SUMMARY AND ANALYSIS OF CLINICAL OBSERVATIONS.

Of the eight cases which form the basis of the present paper, six have been recorded in some detail. In all there was evidence of the presence of a lesion involving the frontal lobe, and in all but one (Case 6) there were also signs of an associated pyramidal lesion. In this one, pyramidal signs never developed, and in the remainder it is probable in some instances at least that grasping and tonic phenomena preceded the appearance of these.

When found, pyramidal signs are such as to indicate a relatively slight impairment of function in this system of neurones. Apraxia was not observed in any of our cases.

Not every one of our cases has shown the full range of grasping and tonic phenomena, and those that have done so have not shown it throughout the whole period of observation. These phenomena develop gradually, reach full development, and then with the progress of the illness they undergo a progressive restriction of range, accompanied by an increasing impairment of consciousness, until finally with the onset of stupor and semi-consciousness, nothing remains but tonic innervation elicited by stretching the muscles involved. Under the conditions of a progressive dissolution of nervous function this component has been the last to disappear.

Of all our cases we may make this generalization, namely, that all showed some unequivocal signs of impairment of psychical function—some signs of dissolution of function in the highest cerebral centres, and we believe this to be an invariable concomitant of grasping movements, and probably also of tonic innervation.

We may most concisely summarize our observations under four clearly marked grades of development which in our experience they have presented.

*I.—The grade of evolution, seen in patients who are relatively little reduced psychically and who can co-operate in their examination.*

In these we have found (1) that when the patient's attention is directed elsewhere, his affected hand closes gently round the examiner's hand when this is slipped into it between thumb and index finger, or when the patient's palm is stroked by the examiner's fingers. When the examiner's fingers are insinuated into the palm from the ulnar side, there is often no trace of grasping.

(2) When the patient is asked to turn his palm upwards and this is then tested systematically—within his sight—with cotton-wool, stroking, pressure and pin-prick, there is no trace of grasping movement.

(3) When the patient is asked to clench his fist, either with the hand empty, or over some object, such as a fountain pen, he can at request open the hand with perfect ease and without delay. Any object that the hand may contain in its grasp drops out freely when it is opened in this way.

(4) Pressure exerted against the palmar aspect of the digits so as to stretch the flexor muscles at once leads to the development of tonic contraction in these muscles, which persists until the fingers are released and stretch of these muscles ceases. This may be elicited either by trying to pull some object out of the patient's grasp, or by inserting a finger or a wooden rod in the crook formed by the semi-flexed fingers and then pulling away.

(5) The patient can easily prevent the occurrence of grasping movements, but once tonic innervation is produced by stretch the patient has no control over it, and only after great and repeated effort can he extend the fingers and release them from the pull.

(6) The patient's hand does not wander towards the examiner's hand when this is offered, nor does it follow this after it has been withdrawn. Tonic innervation appears to be first of the phenomena under consideration to develop.

*II.—The grade of full development—seen in patients whose state of consciousness and intelligence is still sufficient to allow of visual fixation and of some degree of attention.*

In these we have found (1) a grasping of the examiner's hand, when this is within the patient's field of vision, and is offered to the patient or laid beside his affected hand.

(2) In these circumstances the patient's hand and arm move towards the examiner's hand, and follows it when it is withdrawn, whether contact is made with the hand or not.

Both (1) and (2) cease immediately if the patient's eyes are covered.

(3) A grasping of the examiner's hand when this is laid upon the patient's palm, and this whether the patient's eyes be open or shut.

In all three instances the grasping movement is deliberate and very skillfully co-ordinated so as to secure, not merely a hold, but a natural and complete grasp. If means be taken to obstruct this end, the grasping fingers continue to move round the hand until this has been completely and comfortably obtained.

Further in all these instances the patient can prevent the occurrence of the movements when asked to do so. If his attention wanders they restart. This form of grasping is neither "forced" nor involuntary in the strict meaning of these words.

(4) When the patient's open palm is repeatedly touched by the examiner's finger, each touch is followed by a grasping movement of the digits, and when the patient can see the finger his arm may move towards it and may follow it on its retreat. Similarly if in these repeated movements actual contact with the patient's hand is avoided, the latter still makes the movements described so long as the examiner's finger is visible to the patient. If his eyes be covered there is no response except to contact, and then nothing but finger movements.

(5) Systematic sensory testing of the patient's palm as described above evokes no grasping.

(6) Tonic innervation is elicited as described above and only thus.

(7) The patient can open his empty fist with perfect ease.

*III.—Seen in patients who are completely apathetic or mildly stuporose and have ceased to be able to maintain attention—the first grade of dissolution of grasping phenomena.*

(1) and (2) as described under (II) have disappeared.

(3) Present as described above.

(4) Grasping movements of fingers to contact. No movement of arm and no response without contact.

(5) and (6) as described above.

(7) Can open clenched fist easily when able to understand the order.

At this stage catatonia may be present.

*IV.—Final grade of dissolution—seen in patients who are semi-conscious and cannot be roused to attention.*

No grasping movements of any kind. But tonic innervation to stretch persists, though diminished in force.

The observations thus briefly summarized indicate that we are dealing with phenomena of two distinct orders: (1) *a grasping movement* of the fingers, sometimes accompanied by a movement of the whole hand and arm through space, which is highly co-ordinated and capable of a degree of adaptation that unmistakably reveals the activity of the cerebral cortex. The stimulus that evokes the grasping movement of the fingers may be either visual or tactile, but no movement of the limb through space occurs unless the patient can see and fix with his eyes the stimulating object. When the patient's eyes are covered nothing remains but a grasping movement of the stationary hand to tactile stimulation.

Not all visual or tactile stimuli are adequate. For a visual stimulus to be effective it must be such as to make grasping a natural response; the patient must be "offered" the examiner's hand, or this must be laid beside his own. Similarly with tactile stimulation of the hand, moving contacts with the palm such as are made by an offered hand are effective, but systematic sensory examination of the skin of the hand carried out in the manner described above and of an order not naturally productive of a grasping response fails to yield such a response. Finally the grasping movements of hand and the movement of the limb through space can both be prevented by the patient, and are to this extent within his control.

(2) *A tonic contraction* of muscles elicited solely by stretching, and resembling other known tonic reflexes in persisting for as long as the adequate stimulus is kept up. This contraction is wholly outside the patient's voluntary control. It is uniform in character and does not show the highly delicate adaptation to changing circumstances shown by the grasping movements. Unlike the latter it may occur in the semi-conscious patient.

With the question of the localization of the cerebral lesion necessary to allow of the development of the phenomena described we are not specially concerned in this paper. Our own cases, like those of our predecessors, have probably all had a lesion involving the frontal lobe, particularly the frontal and intermediate precentral regions, and the experimental studies in monkeys that are considered in a later chapter confirm the results of clinico-pathological study in this respect. We will make no other comment than to say that in every case, human and animal, in which grasping phenomena or tonic innervation have been seen, the region of the cortical origin of the fronto-pontine path seems to have been involved. Therefore, impairment of function of this neurone system seems to allow the release of the grasping phenomena.

It is true that Bucy [3] has recently recorded two cases of intracranial tumour in which the primary lesion was remote from the frontal lobe. But in each the brain was subjected to severe pressure and internal hydrocephalus was present. The first, and only adequately described case, was one of occipital glioma. Grasping phenomena were a very late development and there was also bilateral external rectus weakness. In these circumstances no neurologist would regard either of these signs as of localizing value.

They merely indicate that under conditions of extreme intracranial hypertension impairment of nervous function spreads far from the site of the initial lesion, a fact with which all neurologists are familiar. They do not conflict with the well-established observation that the lesion underlying grasping phenomena is in the frontal lobe, whether this lesion be a softening or tumour in this situation, or a compression resulting from a tumour elsewhere within the skull.

## CHAPTER III.—THE GRASPING MOVEMENTS CONSIDERED AS VOLITIONAL MOVEMENTS.

Anyone who has carefully observed the grasping movements of the hands that we have described, who has seen the high degree of purpose and skill they display in achieving their object, their perseverance until this has been attained, their subordination to the patient's will—when he can be induced to exert this, and also the extremely specialized stimuli which are necessary to evoke them receives the ineradicable impression that they are voluntary movements. There is an adaptability behind them that allows of no other interpretation, and their dwindling and disappearance with the waning of the patient's consciousness seems to confirm this impression.

There can be no doubt that they do not belong to the class of fixed, inborn reflex reactions of the kind that the researches of Sherrington and other physiologists have made us familiar with, nor with comparable reactions studied clinically in man. And if the identification with these is the basis of the title of "grasp reflex" that has been conferred upon the movements with which we are concerned, then the interpretation is clearly erroneous.

We may say of them that they are volitional movements occurring in individuals whom disease of the brain has reduced to a lower level of internal evolution in respect of their highest motor functions. One of the most striking single instances of the volitional nature of grasping movements was afforded by Case 5. At a period when, for some weeks, he had betrayed no initiative of any kind, and lay speechless and motionless and with fixed stare on his bed, he was examined on many occasions. On one such occasion the examiner approached the bed and was caught by the gaze of the patient, who at once slowly raised his right hand from the bed and offered it to the examiner, obviously to be grasped.

To grasp an object felt by the hand, and then to grasp an object seen, are the first and second stages respectively in the individual's acquired use of the hand. They represent the most deeply organized and therefore most automatic activities of the hand, and their prominence in the circumstances we are considering represents the result of "a "taking to pieces" in the order from the least organized, from the most complex and most voluntary, towards the most organized, most simple and most automatic" (Croonian Lectures, Hughlings Jackson). To label these movements "automatic" in contrast to "voluntary," is merely a matter of terminology, for "most automatic" is nothing but "least voluntary."

It might be urged, however, that to express the situation thus is to do little more than to restate the facts of observation, and that there is nothing in these movements which, under a liberal definition of the term, might not be called reflex. Further, it might be maintained that they are in fact characteristic examples of that group of reactions which Pavlov has called "acquired" or "conditioned" reflexes, and that they differ from the fixed, inborn reflex reactions of the decorticate nervous system only in degree of refinement and not in essential quality. To be precise, the features in which the movements we are considering differ from the latter may be stated as follows: (1) They may be elicited from either of two widely separated receptive fields, visual and tactile; (2) within these fields the adequate stimuli have become highly specialized. An object is not grasped every time it is seen, nor every time it is felt by the hand. It is grasped only when the stimulus is such that grasping is what the individual's experience has taught him to be an appropriate and satisfying response; (3) the response is a far more complex and flexible one than is that of the inborn reflex; and (4) the response can be prevented from occurring by the patient, even when the adequate stimulus has been delivered.

These are indeed the features which Pavlov has described in the reactions he has studied, but we may equally well say of them that they are the characteristic features of cerebral cortical activity in voluntary movement, namely, "reaction to difference, flexibility of response to the same stimuli and habituation to stimuli" [4].

In a recently published critical analysis, Denny Brown, whom we have just cited, has subjected to a very searching criticism the theoretical deductions which Pavlov has drawn from his observations, in particular his use of the terms "reflex" and "inhibition." He points out that to expand the conception of reflex action to include what he prefers to speak of as "conditioned responses" is to make this mean no more than response to stimulus. But this quality may be said to belong to all possible movements. In short, we can speak of these responses as reflex only by depriving this term, and the conception it embodies, of all precise meaning.

This criticism would apply with equal force to a description of the grasping movements as reflex. We add nothing to our knowledge or understanding of them by so naming them, while we confuse the use of what has been, and should remain, a term of precision.

Therefore, we prefer to speak of them as volitional movements. Finally, a word as to nomenclature. These movements are not "forced" in the sense that this description is customarily employed in neurology; as, for example, in respect of the forced movements of some vestibular lesions. Nor are they forced in any figurative sense. Further, the word "groping" implies blindness or darkness, and cannot apply to movements directed by vision, as we have seen the movements so named both necessarily and invariably are. There is little, therefore, to commend the expression "forced grasping and groping," either as scientific, or as usefully descriptive.

*Catatonia and slowness of movement.*—If the subjects who present grasping movements and tonic innervation be observed over a considerable period and until their final lapse into coma before death, it is seen that at a certain level of dissolution of cortical function they become completely apathetic and stuporose, lying silent and motionless in bed, passing urine and fæces under them, and betraying little sign of consciousness beyond occasional movements of the eyes when they see someone passing, or slow movements of the hand and arm to rub nose or face. At this stage in their course catatonia is commonly present, and their movements become extremely slow. It is possible to place a limb in some posture where it remains motionless for one or more minutes.

All these phenomena, grasping movements, catatonia and slowness of movement, express a severe degree of reduction of cerebral function towards the least voluntary and most automatic, and to this category of low-grade volitional activities they all equally belong.

Catatonia was most strikingly observed in Case 4 (H. B.), as is illustrated in fig. 2, in which he is seen to be maintaining positions, passively imposed, of both arm and leg.

## CHAPTER IV.—TONIC INNERVATION CONSIDERED AS A PROPRIOCEPTIVE REFLEX REACTION.

When the Babinski plantar response was first brought to notice, its great practical usefulness as an instrument in diagnosis for long obscured its significance as a fraction of a larger reflex reaction of the lower limb to stimuli of a certain quality. Similarly, the clinical importance of tonic grasping as a "localizing" symptom has distracted attention from the fact that it is but the local expression of a more widespread disorder of neuromuscular activity. It may be said, in fact, that the grasping is fortuitous and does not necessarily provide any clue to the physiological significance of tonic innervation.

It is particularly in the case of the rarely observed tonic innervation of the plantar-flexor muscles of the toes that the term "grasp reflex" is most obviously inadequate and fanciful. (Brain and Curran [2].)

The mechanical arrangements of the foot are such that when all the toes are plantar-flexed they bunch together, and are then capable of holding any appropriately shaped object inserted between them, or put between hallux and sole by the observer. But to suppose that this event has anything to do with grasping in a physiological sense is no more than one of those unconvincing phylogenetic fantasies that see in almost every anomaly of movement the hypothetical activities of our "arboreal ancestors" [16].

We shall therefore adhere to the term "tonic innervation," which lays no undue emphasis upon local phenomena and embodies no hypothetical implications.

The sole adequate stimulus for the production of tonic innervation appears to be stretch of the muscles concerned, a proprioceptive stimulus of the order constantly found in association with tonic reflexes.

Tactile stimulation of the hand we have found to be uniformly ineffective, a result that was to be anticipated in the case of a tonic reflex.

Not only is stimulation of the palm by the patient's own fingers inadequate, but even that delivered by some object held in the grasp is without effect unless this is pulled in such a way as to produce stretch.

While in most of the recorded examples of tonic innervation the cutaneous sensibility of the affected hand has been either normal or but slightly impaired, there are two cases in the literature in which this was not so.

Thus, of Schuster and Pinéas' Case 10, it is said that "Sensibilität für alle Qualitäten ausser Lagegefuhl auf den linke Seite herabgesetzt," while Rhein [11] has recorded in detail a case in which apraxia and tonic innervation (grasping movements not mentioned) occurred in a blind patient whose affected arm was totally deprived of all modes of sensibility.

Too great weight may easily be placed upon cases cited from the literature, but in so far as these two have any bearing upon the question of tactile stimulation of the hand as a stimulus to tonic innervation they are in harmony with our own observations.

The uniformity shown by this reaction in respect of stimulus, receptive field, response and independence of voluntary control shows it to belong to the group of tonic reflexes of the segmental nervous system with which we are familiar both in animals and in man.

Cortical activity plays no part in it, and it stands upon a lower physiological plane than do the grasping movements, the extinction of which it survives.

To passive manipulation, the curious hypertonus of the muscles engaged in tonic innervation differs somewhat from the spasticity of pyramidal lesions. It persists unabated throughout the range of passive movement, and lacks the clasp-knife quality of spasticity, and while the latter remained unchanged throughout the apnœic period in one of our cases, tonic innervation disappeared constantly with apnœa.

Investigation by electrical and myographic methods, or by novocain de-afferentation [15], may throw further light upon its nature and its relation to spasticity.

In none of our cases was tonic innervation of the plantar-flexor muscles observed.

One point remains for mention. It would appear from some descriptions [17] that tonic innervation may ensue upon voluntary contractions and cause delay in relaxation in circumstances where it is not clear that stretch has been operative as a stimulus. Unfortunately for our purpose, the early writers attributed no significance to this factor, did not notice its presence, and in their descriptions give us no idea as to whether or not it was excluded. Thus, the statement that a patient could not open his hand means nothing unless we know the following details: namely, whether stretch was operative, whether the patient understood what was required, whether apraxia of the hand was present, and whether the limb was spastic or not.

Observations repeated many times in our series of cases constantly failed to detect the occurrence of any delay in muscular relaxation when care was taken not to subject the muscles to stretch.

## CHAPTER V.—THE EXPERIMENTALLY PRODUCED "GRASP REFLEX" AND ITS RELATION TO THE PHENOMENA HEREIN DESCRIBED.

The physiologist can determine so many of the conditions of his experiment and can subject his material to such exact study that he undertakes the investigation of this problem with advantages denied to the clinical observer.

This is illustrated by the precision with which experimental study has defined the cerebral lesion necessary to allow of the development of tonic innervation. Unfortunately, the special aspect of the problem with which we are concerned, namely, the analysis of the essential components of grasping phenomena, has received no illumination from this source, except what we may derive by inference.

In the adult macacus monkey, Richter and Hines [9] found that ablation of the intermediate precentral cortex ("premotor area," Brodmann's area 6) is followed constantly by the development of a "grasp reflex." This consists in tonic grasping when the animal is hung by one hand from a horizontal bar, and may be elicited for as long as twenty-one days after operation. The reaction is crossed, but bilateral ablation of the relevant cortical region gives a stronger response in each hand than can be obtained in either by unilateral ablation. Nothing is said in Richter and Hines' brief note about grasping or groping *movements*. It is impossible to say whether in these experiments tactile stimulation of the hand or stretching of the finger flexors provided the adequate stimulus. The method of conducting the observation, namely, hooking the animal's digits over a bar and then releasing the animal, certainly suggests that stretch may have been the essential stimulus.

Richter [6] has also examined the "grasp reflex" in newborn monkeys, and finds that these animals hang for many seconds from a horizontal bar by one hand when this is hooked over the bar in the manner described above. Here also the crucial question of nature of the stimulus is not answered, and there is no mention of grasping or groping movements.

Richter and Paterson [7, 8] have found that appropriate doses of bulbocapnine will produce the same phenomenon in monkeys, the maximum period of hanging being longer in immature than in adult animals. Here, again, nothing is said of any grasping movements; and one is left by these three series of experiments with the impression that all that has been seen is tonic innervation elicited by stretch.

More favourable opportunities of deciding the question appear to have been afforded by some experiments of Fulton, Jacobsen and Kennard [5]. They performed ablation experiments similar to those of Richter and Hines, and their animals showed what have been called "grasping and groping."

Unfortunately these observers have adopted the current hypotheses and nomenclature without question and have made no attempt to study the details of stimulation essential to elicit the phenomena they observed. After bilateral ablation of the frontal and premotor (Brodmann's area 6) cortex they noted (1) that the animal slowly reached for and grasped any object brought within its field of vision; (2) that light stroking of the palmar surface of hand and digits evoked vigorous grasping movements; (3) that a tonic contraction ensued upon this grasp which was of sufficient strength to support the animal's weight for several seconds; (4) that vigorous "grasping" of the foot was seen in one of their two experiments.

We do not learn from these experiments how the tonic grasp was elicited, though it appears probable that here also, hanging the animal from a bar was the procedure adopted. This at once involves the possibility of proprioceptive stimulation. As for the movements of grasping and pursuit, they confirm that vision alone is adequate to elicit them; as to whether they were volitional or reflex we are left in the dark.

If we are justified in drawing any conclusions—other than anatomical—from these physiological experiments, they would be that the observations of Richter and his co-workers indicate that tonic innervation may occur alone without grasping movements, and that stretch is the stimulus necessary to evoke it.

## GENERAL SUMMARY.

The phenomena included under the various headings of "tonic innervation," "the grasp reflex," "forced grasping and groping," and the like are found to be capable of analysis into two distinct and separable components, the one volitional and the other reflex.

(1) The volitional component includes grasping *movements* of the fingers, with which movements of the hand and arm through space are sometimes associated. The stimuli to which they are responses are visual and tactile. Often both are operative, and it is only when the patient has the use of vision that movements of the limb as a whole occur. Tactile stimuli alone evoke nothing but grasping movements of the fingers, the hand and arm remaining still.

On the other hand, visual stimuli acting alone are adequate to evoke the full range of movements.

Only those visual and tactile stimuli are effective to which grasping is a natural and satisfying response. The movements are under the patient's control in that he can prevent their occurrence. They show a delicacy of co-ordination and a capacity for adjustment to changing circumstances that, with the highly specialized stimuli necessary to elicit them, reveal the participation of the cerebral cortex in their production. In these qualities they differ from the fixed, inborn reflexes of the decorticate nervous system, and the term reflex cannot be rightly applied to them. They are in fact volitional movements occurring in individuals whose psychomotor functions have been reduced by disease of the brain to the production of the "least voluntary" and "most automatic" movements. They are not "forced," or involuntary. They occur only in the conscious patient, and disappear with the development of stupor or coma.

(2) The reflex component consists in the tonic innervation of muscles when, and only when, these are subjected to the proprioceptive stimulus of stretch. Tactile or visual stimuli are not adequate to produce it. It may occur in the conscious or in the unconscious patient, and it is entirely outside the patient's control. The stimulus and the response are fixed and uniform and indicate that we are dealing with a true tonic reflex of the segmental nervous system, and one in which the cerebral cortex plays no part.

Tonic innervation of the grasping movement occurs only when the grasping muscles are subjected to stretch, as when the attempt is made to extract some object held in the grasping hand. When all grasping movements have disappeared with the waning of consciousness, tonic innervation persists and can be elicited by sudden passive extension of the fingers.

The tonic grasp is only the local expression of a more widespread mode of innervation of the muscles, and is in this sense a fortuitous phenomenon that does not necessarily provide any clue as to the origin or significance of tonic innervation. For this reason the term "grasp reflex" is undesirable as conveying a false emphasis upon what is no more than a local manifestation. This is particularly the case when the term is applied to tonic innervation of the plantar-flexors of the foot described by some writers which, even when dressed in the language of metaphor, is not obviously a grasp.

The experimental studies of grasping phenomena in so far as they throw any light upon the problem considered in this paper, suggest that tonic innervation is a true proprioceptive tonic reflex, of which grasping movements are an uncertain concomitant.

The lesions which allow of the development of grasping movements and of tonic innervation appear to be situated in the frontal lobe, anterior to the excitable motor cortex and adjacent to the longitudinal fissure. Experimental studies on monkeys indicate that the intermediate precentral region ("premotor area," Brodmann's area 6) is the precise localization of the essential lesion.

In respect of nomenclature, the two separate components described should be dealt with separately. For the volitional component no term more precise than that of "grasping movements" is necessary or justified, since these movements are neither reflex, nor "forced." For the reflex component, "tonic innervation" remains the most suitable term in the present state of knowledge.

To those members of the Medical Staff of the National Hospital who have allowed us to examine and record their cases, we express our thanks.

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# THE RATE OF CONDUCTION AND REFRACTORY PERIOD OF THE HUMAN SENSORY NEURONE.

BY F. GOLLA AND S. ANTONOVITCH.

*(From the Central Pathological Laboratory of the London County Mental Hospitals.)*

SUCH investigations as have been conducted on the physiology of the nervous system of the intact human being have been almost entirely confined to the efferent portion of the nervous system, or at any rate to such experiments as may be checked by the muscular response.

On the sensory side we have, however, means of judging the effect of excitations by our sensory impressions which are intrinsically more delicate than the investigation of motor responses and allow absolutely normal physiological conditions instead of the extensive dissection and exposure necessary to allow records of sensory processes to be obtained by amplification of the electrical response. It is hoped that the experiments to be described will permit the evaluation of the effects of drugs and states of chemical equilibrium under conditions which could not possibly be so favourable in animal experiments.

*Method.*—It was necessary to deliver two successive stimuli at variable intervals. The stimuli had to be of such short duration that the time through which they acted was negligible and the time intervals determinable within 0·1 sigma. A Lucas pendulum was used, so adjusted as to allow determinations of the time relations within 0·1 sigma. The velocity of the pendulum when used in conjunction with the electrical contacts employed in these experiments was determined both before and after a series of experiments, using a string galvanometer as recorder in the usual manner. The variations of the velocity were found to be negligible. The type of key originally designed by Lucas for break shocks was modified in such a way that only an instantaneous closure of the circuit occurred when the pendulum struck the steel pin of the key (fig. 1). To effect this the striker of the pendulum was connected with one arm of the circuit, the other connection being made to the knife edge on which the steel pin rests. The circuit is closed for the very brief interval of time elapsing between the moment when the striker first makes contact with the steel pin, and that when the pin is pushed by the striker from the knife edge. The time during which the current is closed is negligible for the purposes of these experiments, being less than 0·01 sigma. The very small intervals during which the circuits were closed were found not to be absolutely equal, and this inequality manifested itself as a difference in intensity of the stimulus. The stimuli led off from the two keys had therefore to be equalized when the electrodes were applied by the use of non-inductive resistances. A battery of accumulators of 120 volts and a suitable potentiometer completed the circuit.

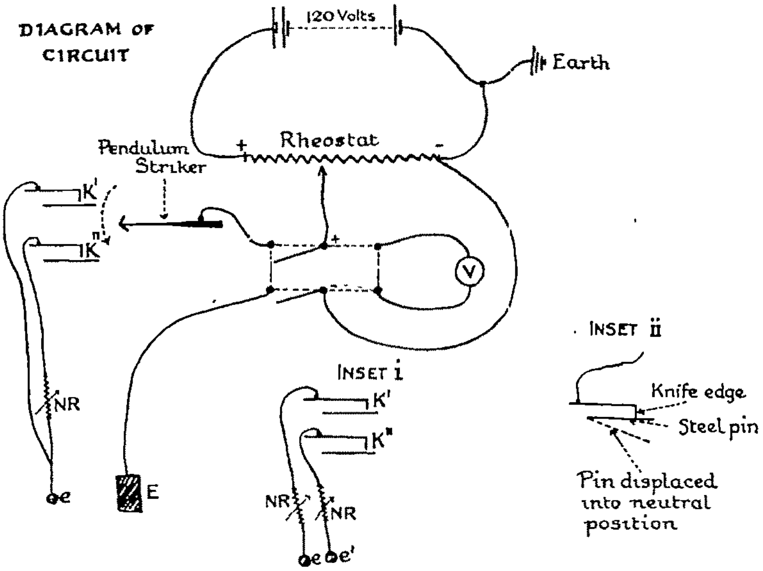

FIG. 1.—The Lucas Pendulum is represented diagrammatically as two keys (K', K'') and the striker K'' is movable along a graduated scale, so that the interval between the two stimuli can be varied and accurately determined. In the diagram both stimuli would be applied at the same point on the skin. Inset i shows the arrangement by which two distant points can be stimulated successively. E = indifferent electrode. NR = non-inductive resistance. V = voltmeter. Inset ii shows a key in detail.

The electrodes used were at first similar to the silver non-polarizable electrode of Bourguignon, the neutral electrode being about 8 sq. cm. in size and the stimulating electrodes having each a surface of one square centimetre. It was subsequently found that equally good results were obtained with zinc electrodes. When the successive stimuli were delivered at one spot a common electrode was used.

The choice of a suitable subject must be a matter of great importance if the results here presented are to be verified. These investigations having been begun with one of the authors as a subject, we have continued to depend mainly on the same subject throughout these experiments. All the conclusions, were, however, verified on a laboratory assistant who proved to be a good and objectively minded witness. Two other youths proved, however, to be useless as subjects, at any rate without more training than we had leisure to give. So far as it was possible for us to judge, their chief faults were inattention and a tendency to guess when not sure.

From introspection it is possible in some degree to define the state of mind necessary for a successful result as one in which in describing a sensation all qualities other than the particular one studied for the purpose of the experiment are ignored. Thus, in judging summation, nothing but the magnitude of the sensation must be considered and spatial and temporal references must be neglected. In judging the presence or absence of multiplicity of the stimulus, the temporal reference must be considered, to the exclusion of magnitude and localization. The fluctuating qualities of the local sign present a very puzzling and disturbing element. It would appear that within a small area underlying the stimulating electrode there is a continuous fluctuation of the skin spot to which the stimulus is assigned. Any two stimuli following each other at a sufficiently brief interval are invariably assigned to the same spot, but after an interval of a minute a second pair may appear to affect a spot which is felt to be at some little distance away, and the second pair appears to possess a different affective tone to the first. It is doubtful how far these variations are due to alterations of skin conductivity of the same nature as the so-called psychogalvanic reflex, which is conditioned by concomitant alterations of the affective tone. Whatever be the interpretation of these fluctuations of affective tone and local sign, their occurrence renders it necessary for the stimuli which are being compared to be delivered in pairs and for the observer to pronounce judgment on each pair without reference to any preceding pair. This method of pairing obviously increases very greatly the number of stimuli that have to be administered, and makes great demands on the endurance of the subject. It was found that experiments were greatly facilitated when a warning preceded the delivery of the stimulus, and this was very conveniently rendered by the noise of setting the keys before each swing of the pendulum. These movements had to be performed with a strict observance of tempo—any irregularities in the time interval between the warning signal and the stimulus caused disturbance of the subject's attention.

*The refractory period of the afferent nerve.*—In the first instance this was determined in the ulnar nerve. The stimulating electrode connected with the keys K′ and K″ was firmly bound on to the skin overlying the nerve at the ulnar groove by sticking-plaster. The large neutral electrode was applied to the lower dorsal region. In other experiments the supraorbital nerve was selected at its point of emergence from the supraorbital groove, and in another series the musculocutaneous nerve as it winds round the head of the fibula. From all these three points identical results were obtained. There is, of course, no reason why stimulation of the cutaneous nerve at any place should not yield equally satisfactory results, and this was found to be roughly true, but the points enumerated had been selected in the course of some earlier experiments directed to other purposes and were adhered to as a matter of convenience. The voltage was adjusted to give two plainly perceptible stimuli when the keys K′ and K″ were separately closed by the pendulum. The stimuli were then adjusted so as to be of equal intensity by means of the non-inductive resistances. This was necessary, as intrinsic differences in the tension of the springs of the two keys by causing minute differences in the time of closure rarely gave an equal strength of stimulus from either circuit. When the stimuli were judged to be of equal intensity, the voltage was lowered till both stimuli were just a little above the threshold of sensibility. The exact intensity of stimulus for optimum results can only be settled by the experience of the subject, in view of the impossibility of gauging the skin resistance to the constant current owing to polarization. The moving key K″ is now adjusted so that a double stimulus is given practically simultaneously, and this is compared with a single stimulus from one or other of the two circuits. So long as the second stimulus falls within the total refractory period following the first, the double stimulus will be judged to cause a sensation equal in intensity to that of the single stimulus. When the key K″ has been moved to a point at which the second stimulus falls in the partial refractory period of the first, it will be noted that the double stimulus effect, owing to summation, is now slightly greater than the effect of the single stimulus. This point, marking the end of the period of the total refractory state, can be determined within 0·1 sigma. As the second stimulus is moved further and further through the partial refractory period, a progressive increase of the strength of the double stimulus effect is noted, and the increase can be registered step by step within limits of 0·5 sigma. Finally, a point of maximum sensation is reached, and for some time the double stimulus continues to give effects of uniform intensity while the second stimulus is being moved further and further from the first. When an interval of about 12 sigma between the stimuli is reached, the intensity of the sensation tends to diminish and, as will be seen later, this point corresponds with the sensation of reduplication. This diminution of intensity is, however, very difficult to localize in time with the degree of accuracy corresponding to that of the points for the refractory period.

The total and partial refractory periods here determined are undoubtedly those of the afferent nerve itself. They correspond closely to the total and partial refractory periods observed when the ulnar nerve is stimulated by somewhat stronger currents and the resultant contraction of the abductor minimi digiti is mechanically recorded (fig. 2). It will be observed that the total refractory period is appreciably more prolonged in the motor nerve, but it must be borne in mind that the mechanical record offers a far coarser testimony than that of sensation.

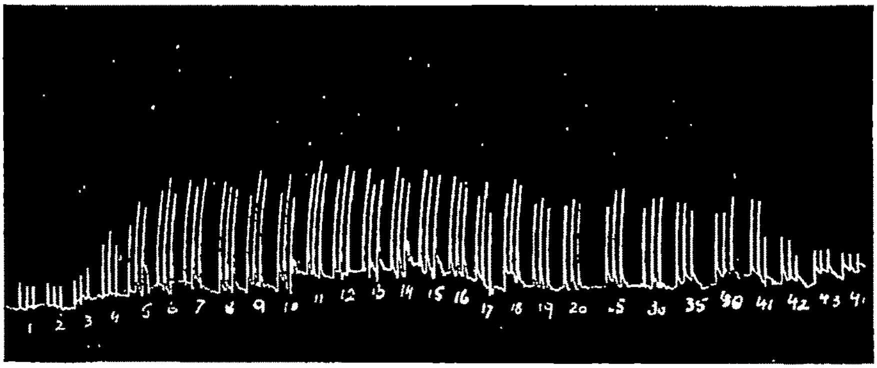

FIG. 2.—Tracing of movements of little finger in response to stimulation of ulnar nerve at olecranon. Figures indicate scale-reading on Lucas Pendulum. Three contractions are recorded for each reading.

In the tracing the contraction of abductor minimi digiti is recorded to stimulation of the ulnar nerve at the olecranon by pairs of stimuli with lengthening interval between the stimuli.

The contractions are recorded in groups of three for each stimulus interval. The figures refer to the instrumental scale. Summation begins with a stimulation interval of 2·5 sigma, which represents the length of the total refractory period. It reaches a maximum at about 5 sigma stimulus interval which represents the end of the partial refractory period. Summation begins to subside at a stimulus interval of about 13 sigma.

The absence of any objective value for the intensity of sensation makes it impossible to represent summation graphically. The following table represents the time relations of the total and partial refractory periods.

| | Stimulation interval | Sensation of double stimulus |
|---|---|---|
| Total refractory period .. | 0·1 sigma | Same as single |
| | 0·2 ,, | ,, ,, ,, |
| | 0·5 ,, | ,, ,, ,, |
| | 1·0 ,, | ,, ,, ,, |
| | 1·5 ,, | ,, ,, ,, |
| | 1·6 ,, | ,, ,, ,, |
| | 1·7 ,, | ,, ,, ,, |
| Partial refractory period .. | 1·8 ,, | Greater than single |
| | 2·5 ,, | Greater than at 1·8 sigma |
| | 3·5 ,, | Greater than at 2·5 sigma |
| | 4·0 ,, | Same as at 3·5 sigma |
| | 6·0 ,, | Same as at 3·5 sigma |
| | 8·0 ,, | Same as at 3·5 sigma |
| Onset of sensation of reduplication .. .. .. | 12·0 ,, | Less than at 3·5 sigma but greater than single |

Another method of demonstrating the total refractory period is to diminish the intensity of the two successive stimuli till they are each just below the threshold of sensation. If the two stimuli be then delivered together within the total refractory period no sensation will occur, and the time value for the onset of summation at the expiration of the total refractory period can be determined very sharply by noting the first appearance of sensation. The curve of summation is, however, less easily followed when working with such minimal sensations.

The values obtained for the total and partial refractory periods and for summation apply obviously to the sensory nerve in the first instance. There is, however, no evidence that will allow us to decide how far the time values assigned to the refractory period and summation apply to superior neurones in the nervous system. It is by no means inconceivable that the greater or lesser impulses conditioned by the refractory period of the lower sensory neurone are translated by superior neurones possessing entirely different refractory and summation periods. Should this be so, however, the universal application of the all or none law to the neurones of the central nervous system would then make it necessary to postulate that the larger and smaller responses conditioned by the total and partial refractory periods of the lower motor neurone are transformed into repetitive discharges of varying frequency when the impulse is passed on to the superior neurone, possessing a different refractory period.

*The reduplication of sensation.*—When two successive stimuli are separated by an interval of 10·6 sigma the sensation is found to have a multiple or manifold character as if resolvable into two or more separate stimuli. We have termed this new sensation "reduplication," but it should be understood that introspective analysis does not allow the subject to state clearly that the new sensation is composed of two separate sensations. All that he can say is that it appears multiple, but whether the multiplicity is composed of two or three separate stimuli cannot be definitely stated at this time interval. It is not till an interval between the stimuli of 27 sigma is reached that the double nature of the sensation becomes quite definite. The incidence of the first signs of reduplication occurred constantly in both observers at an interval of 10·6 sigma between the stimuli. The judgment error in either direction was not found to exceed 0·5 sigma. As in the case of summation the results were the same when obtained from the observation of the dull touch-like sensations in the forearm or the pain-like sensations from the wrist and finger.

If the two stimuli be applied by two separate electrodes placed side by side, the results obtained are identical with those from a single electrode. The appearance at this specific time interval of the sensation of reduplication does not therefore depend on the stimulation of identical nerve fibres. Further it does not depend on the stimulation of identical nerves. If one electrode stimulates the tip of the little finger (ulnar nerve) and the other the tip of the index finger (median nerve) the time relationship of the occurrence of reduplication remains unaltered, although judgment becomes more difficult for the subject. If corresponding fingers on the right and left hands be selected for successive stimulation it was found that judgment of the exact point of reduplication of the sensation became extremely difficult and it was impossible with precision to fix the reduplication point which occurred at a stimulus interval of about 25 to 30 sigma. Similar lengthening of the reduplication time was noted when the homolateral arm and leg were stimulated.

Certain inferences may be drawn from the foregoing experiments. The central nervous mechanism serving the sensation of reduplication has the same functional time relations whether both successive stimuli be applied to the same nerve fibre, to different nerve fibres, or to different but adjacent peripheral nerves. The sensory change interpreted as reduplication corresponds very closely in its stimulus interval to that at which sensory summation appears to wane. These functional time relations correspond very closely to those observed in the muscular effector organ. Fig. 2 shows that when the ulnar is stimulated the waning of muscular summation in the abductor minimi digiti occurs at about the same stimulus time interval as does the waning of sensory summation and the appearance of reduplication on the sensory side.

When a double stimulus is felt as such we are entitled to assume that we have a measurement of what must be the greatest possible duration of the refractory period of the central receptor neurones. These are successively responsible for the ultimate presentation of the sensation at the level at which judgment is pronounced, but we are by no means entitled to assume that we have also a measure of the lower limits of this period. The ultimate datum, reduplication or non-reduplication, is not a pure sensation, but a judgment involving reference to the ideas of oneness or twoness, which again in this connection probably have temporal connotations. It may well be that the whole of this complex mechanism requires for its functioning the relatively large stimulus interval of 11 sigma, whilst individual neurones in any part of the nervous system respond to stimuli at the same interval as that found for the refractory period of the lower sensory neurone.

The fact that Cooper and Denny Brown were able to show that the cortex in the cat can follow a maximum stimulation by break shocks at the rate of 180 in the second would indicate a fairly close correspondence with the refractory period determined in our experiments for the lower sensory neurone.

The diminution of the intensity of the sensation beginning at the stimulus interval of 12 sigma continues through increasing stimulus intervals, fading gradually into the intensity of the single sensation when each stimulus is felt as absolutely discrete.

*The velocity of conduction in afferent nerves.*—The fact that the judgment of the point of reduplication is effected with equal accuracy when the stimuli are administered to separate nerve fibres makes it possible to utilize the reduplication point for the estimation of the velocity of conduction of afferent nerves.

If we know the minimum stimulus interval at which two successive stimuli give a reduplicated response when both stimuli are administered at the same spot on the periphery of a sensory nerve, it is sufficient, in order to obtain the velocity of conduction, for the reduplication stimulus interval to be determined when the two electrodes are separated by shifting the second stimulating electrode a known distance along the course of the nerve. The velocity is obviously most easily estimated when dealing with a subcutaneous sensory nerve with straight course permitting some degree of accuracy in linear measurement. The ulnar is the best nerve fulfilling these requirements. The electrode of B circuit conveying the second stimulus is strapped on to the ulnar nerve at the olecranon. The electrode of A circuit conveying the first stimulus is successively fixed in two positions, first over the ulnar nerve at the wrist and secondly on the palmar side of the terminal phalanx of the little finger. The length of nerve lying between these three points may be estimated with a possible error of about ±5 per cent. It has already been stated that when the same point of skin is subjected to a double stimulus, the minimum reduplication time is the same and determinable within 0·5 sigma wherever the selected point may be, and that when two points of skin are taken for the two respective stimuli the reduplication time can be determined with equal accuracy.

It was found that the reduplication time with the electrodes at the olecranon and the wrist could be determined within ±0·5 sigma. The reduplication time when the electrodes were on the olecranon and the terminal phalanx of the little finger was more difficult to determine owing probably to the qualitative difference between the finger sensation which has a painful tone, and the olecranon which has a purely tactile tone, at the current strength employed for these experiments. The constant error in the finger olecranon experiments was ±0·8 sigma.

The proximal electrode is connected with the movable key. When the two keys are struck simultaneously it is obvious that the stimulus from the distal electrode will reach the central nervous system after the stimulus from the proximal electrode by such a period of time as the impulse has taken to traverse the nerve tract lying between the two electrodes. If by shifting the movable key the proximal stimulus be progressively retarded a point will be arrived at when the stimuli are judged to be reduplicated.

| Subject | Stimulus interval for reduplication | | Nerve length | Velocity of conduction |
|---|---|---|---|---|
| G. | Both electrodes on same spot | = 0·0106 secs. | — | — |
| | Electrodes on wrist and olecranon | = 0·0146 ,, | 30·2 cm. | 75 m. per sec. |
| | Electrodes on terminal phalanx and olecranon | = 0·0170 ,, | 46·5 cm. | 72 m. per sec. |
| H. | Both electrodes on same spot | = 0·0106 ,, | — | — |
| | Electrodes on wrist and olecranon | = 0·0188 ,, | 26 cm. | 81 m. per sec. |
| | Electrodes on terminal phalanx and olecranon | = 0·0162 ,, | 42·5 cm. | 74 m. per sec. |

The velocity assigned to the ulnar afferent nerve fibres would appear to be between 72 and 81 m. per second from the many hundreds of observations on the two subjects G and H. The possible error assessed from variations in the summation time and the difficulty of assigning an exact length to the nerve tract would appear to be about ± 5 per cent. These estimations of velocity are therefore somewhat less accurate than those which we previously published for the motor fibres of the ulnar nerve. In these the velocity of conduction in subject G was found to be 37·8 m. per second with an estimated probable error of ± 1 per cent;

The determination of the velocity of conduction of the afferent impulse in the human subject has given varying results. Attempts to estimate the velocity of sensory impulses based on reaction times cannot by their nature give results of any significance in the normal subject. The only attempt to investigate the velocity of the sensory impulse by objective methods has been that of Schäffer, who recorded the electromyogram of the electrically conditioned patellar reflex. He assigned a velocity of 54·4 m. per second to the motor nerve and 59·4 m. per second to the sensory nerve. His results cannot, however, claim serious consideration, they vary between 48 m. and 73 m. per second, the largest result being 52 per cent. greater than the smallest.

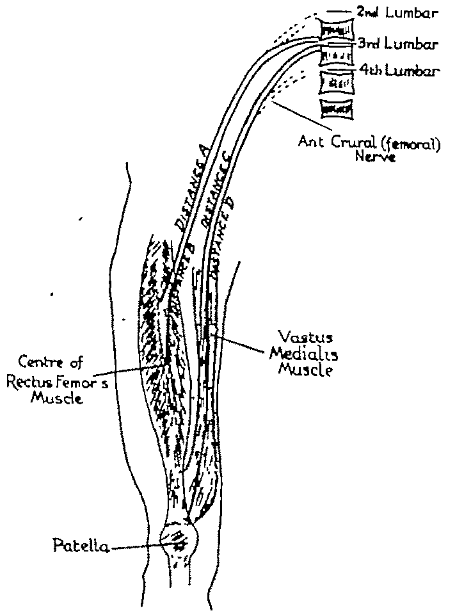

FIG. 3.—A, length of the nerve to rectus femoris to its insertion into the muscle. B, distance of A + distance between the point of insertion of the nerve and the centre of the rectus femoris muscle (midway between origin and insertion). C, length of the nerve to vastus medialis to its insertion into the muscle. D, distance of C + distance between the point of insertion of the nerve and the upper border of the patella.

If the results here recorded be valid it would appear that the velocity of the afferent nerve is about twice that of the motor nerve. Such a conclusion seems inevitable if we are to accept the velocity of 37·8 m. per second for the motor nerve and to regard the knee-jerk as a stretch reflex.

The length of nerve involved in the patella reflex has been investigated by F. A. Hoffmann, who obtained values between 110 cm. to

133 cm. in the living subject. Professor Le Gros Clark very kindly made the following series of observations for us on a series of cadavers.

The nerves were measured from the intervertebral foramen transmitting the third lumbar nerve along the trunks of the lumbar plexus to the point where the peripheral branch was inserted into the muscle. Measurements were also taken of the muscles as shown below (fig. 3).

| | 1<br>Height<br>5 0½ | 2<br>Height<br>5.11½ | 3<br>Height<br>5.2 | 4<br>Height<br>5.3½ | 5<br>Height<br>5 7 |
|---|---|---|---|---|---|
| A | 291 mm. | 391 mm. | 316 mm. | 306 mm. | 281 mm. |
| B | 419 ,, | 534 ,, | 382 ,, | 371 ,, | 365 ,, |
| C | 461 ,, | 569 ,, | 509 ,, | 456 ,, | 581 ,, |
| D | 679 ,, | 716 ,, | 599 ,, | 603 ,, | 601 ,, |

In the case of a man of 5 ft. 11½ in., repeated observations of the total reflex time of the knee-jerk gave values of between 24 and 26 sigma. If distance B to the middle of the rectus femoris be assigned to the efferent conduction path the time taken by an impulse travelling at the rate of 37·8 m. per second would be 14 sigma. If distance D from the patella be assigned to the afferent path the time taken by an impulse travelling at the rate of 75 m. per second would be 9 sigma; the total estimated conduction time being 23 sigma when the observed time was 24-26 sigma, thus allowing about 3 sigma as the latent period for the affector organ and no measurable time for the synapse. If the stretch receptors be placed somewhere about the middle of the quadriceps the estimated conduction time may be reduced to 21 sigma. It would appear, therefore, that assuming the absolute accuracy of the value of 37·8 m. per second for the efferent velocity, the velocity of the afferent impulse cannot be less than that deduced from the foregoing experiments.

Felix observed the reflex time of the reflex contraction of the foot muscles when the afferent nerve is stimulated at the malleolus. A large number of experiments in a series of short and tall subjects gave an average reflex time of 46 sigma for a reflex involving an estimated nerve-path of 228 cm. Apart from the impossibility of accurately measuring the nerve-length, the electromyogram is difficult to read accurately owing to the proximity of the area of stimulation to the galvanometer electrodes and the probable error is about ± 5 per cent. Felix could not by his procedure differentiate between efferent and afferent conduction and assigns a mean velocity of conduction to the entire nerve-tract. If, however, our value of 38 m. per second for the efferent nerve be assumed to be correct, the 114 cm. efferent portion of the reflex tract will be traversed in 30 sigma, and this leaves 16 sigma for the sensory conduction time, giving a velocity of 70 m. per second for the afferent nerve. A figure which is, within the limits of error, compatible with our estimations.

That a slowing of the nervous impulse takes place towards the periphery was first suggested by Helmholtz and recent work by Felix tends to confirm this suggestion. His experiments do not, however, indicate that such difference of velocity of conduction between the central and peripheral portions of the nerve-trunk is sufficient to affect sensibly these results.

*Conclusions.*—A method is described for the investigation of certain functions of the sensory portion of the nervous system in the human subject.

The refractory period of various sensory nerves has been determined. The total refractory period lasted 1·7 sigma, the partial refractory period 2·3 sigma. A gradual increase of the sensory response was noted when the second stimulus fell within the partial refractory period of the first and the stimulation interval was gradually increased.

A sensation of reduplication was noted when the two stimuli were 11 sigma apart.

The sensation of reduplication was accompanied by a diminution of the intensity of sensation.

Using the method of determining the point of reduplication it was found possible to estimate the velocity of conduction of an afferent impulse in the ulnar nerve. The mean velocity of conduction was found to be 75 m. per second.

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# ON THE CONNECTIONS OF THE MEDIAL CELL GROUPS OF THE THALAMUS.

BY W. E. LE GROS CLARK AND R. H. BOGGON.
*(Department of Anatomy, St. Thomas's Hospital Medical School, London.)*

In recent years, anatomical studies of the mammalian diencephalon have led to a much more satisfactory definition of the medially situated nuclei of the thalamus than had previously been attained. It is desirable now to follow up these morphological studies by an experimental investigation of the fibre connections of these elements. This paper is a report on a series of experiments which have been carried out with this end in view.

## METHODS.

The methods used in this investigation were similar to those described by us in a previous communication on the connections of the anterior nucleus (Clark and Boggon, 1933). Small electrolytic lesions were produced in the thalamus of the cat with a Clarke-Horsley stereotaxic instrument, and the course of the degenerated fibres studied by the Marchi method. Where a thalamo-cortical connection was thus found, this was corroborated in the cat and the rat by making lesions in the corresponding cortical region and studying the cellular atrophy in the thalamus which ensued after an interval of approximately three months.

For the purposes of our experiments ether anæsthesia proved the best, but it requires considerable skill to keep the animal at the correct level of anæsthesia during the whole of the operation. No abnormal bleeding was followed by its use. In our hands intraperitoneal dial was unsuitable, as a dose sufficient to keep the animal unconscious and quiet delayed the return of consciousness for an inconveniently long period.

We have found the papers by Rioch on the carnivore diencephalon (1929 and 1931), and a recent paper by Ingram, Hannett and Ranson (1932) of great value in delineating the thalamic nuclei in our sections of the cat's brain.

## EXPERIMENTS.

*Cat* 6.—Operated April 8, killed April 26.

The right cerebellar fossa was opened and the Clarke-Horsley apparatus applied to the head. The electrode was inserted 12 mm. in front of the central point, 1½ mm. to the left, and 5 mm. upwards (instrumental error being allowed for). A current of 5 milliampères was allowed to flow for five minutes.

*Microscopical examination.*—The extent and position of the electrolytic lesion may be seen by reference to fig. 1. It lies mainly to the left of the mid-line in the rostral part of the thalamus, encroaching very slightly on the right wall of the third ventricle. It involves here on the left side the periventricular system, the most medially situated fasciculi of the inferior thalamic peduncle, the most medial part of the anteromedial nucleus, and close to the mid-line the commissura interanterodorsalis. More rostrally, the lesion extends into the most medial fasciculi of the left descending fornix column and into the most medially situated fibres of the inferior thalamic peduncle of the right side.

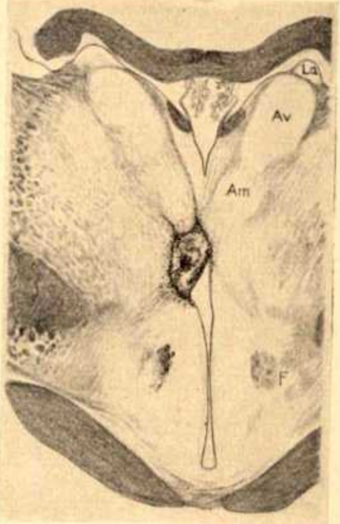

FIG. 1.—Section through the rostral part of the thalamus of Cat 6, showing the lesion. × 4. Am, Anteromedial nucleus. Av, Anteroventral nucleus. F, Fornix. La, Lateral nucleus.

From the site of the lesion on the left side of the mid-line, degenerated fibres extend dorsally to the stria medullaris, and ventrally in the inferior peduncle and fornix. None of the degenerated fornix fibres run into the pre-optic region. The fibres of the interanterodorsal commissure contain scattered Marchi granules which can be followed up into the anterodorsal nucleus of either side. On the other hand the anteroventral nucleus is quite clear of osmic deposit. There is no Marchi degeneration in the internal capsule or in any part of the cerebral cortex.

Caudally at the level of the middle of the thalamus, the lesion produced by the track of the needle lies immediately to the left of the mid-line and medial to the mammillo-thalamic bundle, cutting across the periventricular system of fibres. Here a few fine fasciculi of degenerated fibres extend up in the periventricular system to the paratænial nucleus, and also into the dorsomedial nucleus, the greater part of which, on the left side, is finely sprinked with osmic granules. A few degenerated fibres can also be followed ventralwards in the periventricular system for a very short distance, but none are seen to reach down into the hypothalamus. From the site of the lesion at this level Marchi granules extend for a short distance medially and laterally in the fibres which run transversely in the region of the nucleus centralis medius.

Thus, in this specimen, the Marchi degeneration resulting from a lesion close to the mid-line of the thalamus is confined to immediately neighbouring regions, with the exception of the degenerated fibres in the fornix and the inferior peduncle of the thalamus. The distinct degeneration in the fine fibres pervading the dorsomedial nucleus provides evidence of an ascending connection between the periventricular system of fibres and this nucleus.

*Cat* 7.—Operated April 12, killed April 29.

In this case the electrode was inserted to a point 12 mm. anterior to the central point, 1½ mm. to the left of the mid-line, and 5 mm. above the horizontal plane. A current of 5 milliampères was allowed to flow for five minutes.

*Microscopical examination.*—The electrolytic lesion was found to be situated in the upper end of the left habenulo-peduncular tract reaching dorsally to a point 1·5 mm. below the caudal extremity of the habenular ganglion, and medially to about 1 mm. from the mid-line. It measures just under 3 mm. in vertical and 2 mm. in transverse diameter. The medial margin of the central median nucleus is involved, as well as some of the fibres of the periventricular system at this level (fig. 2). More caudally, the lesion extends into the fibres which are coursing dorsomedially into the posterior commissure, and the latter is densely stained with the osmic acid. Rostrally, the lesion does not reach forward further than the level of the habenulo-peduncular tract.

Degenerated fibres radiate out from the site of the lesion in all directions, but none can be traced for more than a short distance (except, of course, those in Meynert's bundle). Some pass dorsally into the substance of the pretectal nucleus, laterally into the centre median nucleus and the medial margin of the lateral nucleus, and ventrolaterally into the most medial part of the ventral nucleus (nucleus ventralis, pars medialis). Others run ventrally in the periventricular system, but do not extend into the hypothalamus.

In sections passing through the middle of the thalamus rostral to the lesion, the medial medullary lamina contains scattered Marchi granules which permeate the substance of the nucleus paracentralis and nucleus centralis lateralis, and some fine degenerated fibres are seen to cross over through the nucleus centralis medius to reach the medial medullary lamina of the opposite side. It was not possible to determine with certainty to which nuclei these intralaminar fibres are specifically related.

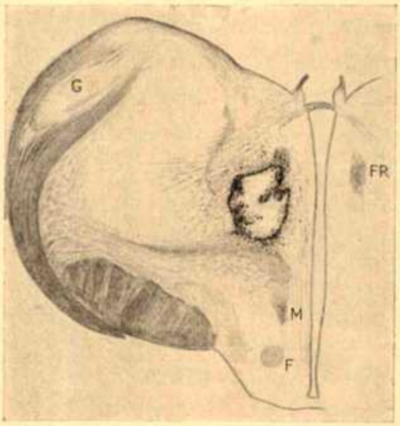

FIG. 2.—Section through the caudal part of the thalamus of Cat 7, showing the lesion. × 4. F, Fornix. FR, Fasciculus retroflexus. G, Lateral geniculate body. M, Mammillo-thalamic tract.

Sections through the anterior part of the thalamus—at the level of the anterior nucleus—show no definite Marchi degeneration. In none of the sections (including those taken through the frontal lobes) were degenerated fibres found to reach the internal capsule or the cerebral cortex.

This experiment indicates that, with the possible exception of fibres passing into the mesencephalon (for the investigation of which the lesion was not suitable), the efferent connections of the centre median nucleus are entirely intrathalamic.

*Cat* 19. Operated September 20, killed October 5. The electrode was inserted in the mid-line to reach 9 mm. in front of the central point and 4 mm. above the transverse plane. A current of 7 milliampères was allowed to flow for seven minutes.

*Microscopical examination.*—The most caudal section of the series shows the track of the needle passing through the cerebral aqueduct and involving here the most caudal and ventral fibres of the posterior commissure. Degenerated fibres of this commissure extend out on either side into the pretectal nucleus, the nucleus of the posterior commissure, and further ventrally into the dorsal part of the tegmentum. The habenulo-peduncular tracts are filled with Marchi granules as the result of their partial involvement by the lesion at their upper extremity. There is no osmic deposit in the cerebral peduncles. At the caudal end of the thalamus the track of the needle passes forwards in the mid-line at the upper margin on the third ventricle immediately ventral to the habenular ganglion. From the site of this small lesion very fine degenerated fibres can be traced down in the periventricular system as far as the level of the ventral medullary lamina, but not into the hypothalamus.

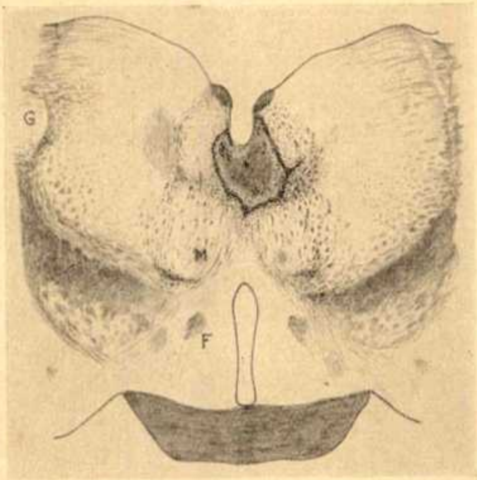

FIG. 3.—Section through the middle of the thalamus of Cat 19, showing the lesion. × 4. F, Fornix. G, Lateral geniculate body. M, Mammillo-thalamic tract.

The electrolytic lesion lies in the middle of the thalamus at the level of sections passing through the optic chiasma and the rostral pole of the lateral geniculate body (fig. 3). It is in the mid-line, extending from the stria medullaris to the ventral margin of the nucleus centralis medius, measuring 3 mm. in vertical and 2·4 mm. in transverse diameter. As may be seen from the figure, the lesion involves on the right side practically the entire dorsomedial nucleus, as well as the medial margin of the nucleus centralis lateralis, while on the left side it involves approximately the medial half of the dorsomedial nucleus. It extends forwards to the rostral extremity of the dorsomedial nucleus, cutting into the medial olfacto-habenular tract and the commissura interanterodorsalis, but does not reach the anterior nuclei. It should be noted that nowhere does the lesion extend lateral to the medial medullary lamina.

From the site of the lesion, fascicles of degenerated fibres run through the medial medullary lamina, and ventrally in the inferior thalamic radiations mainly to the lateral side of the mammillo-thalamic tract. A fine deposit of Marchi granules is also present in the commissural fibres coursing through the nucleus centralis medius and nucleus paracentralis, reaching out to the medial part of the nucleus centralis lateralis. The degenerated fibres of the inferior thalamic radiations are more numerous on the right side and run downwards and forwards to collect at the medial extremity of the internal capsule. Further forwards, in sections passing through the caudal part of the septum, the Marchi staining of these fibres is very distinct and is localized to the fasciculi which lie immediately dorsal to the intermediate root of the olfactory tract. The grouping of the degenerated fibres in sections through the rostral part of the septum is shown in fig. 4A. It will be noted that they reach down close to the basal surface of the brain and, at this level, some of them run laterally through the extreme anterior end of the lenticular nucleus to reach the external capsule. There is no Marchi staining in the anterior commissure, nor in the caudate nucleus. In sections further forwards—through the frontal pole of the hemisphere—the degenerated fibres are seen in the most ventral part of the centrum ovale, extending up almost to the floor of the lateral ventricle. Here, also, they can be seen extending into the deeper layers of the cortex of the gyrus proreus (which are sprinkled with a very fine Marchi deposit), and reaching from the upper lip of the sulcus presylvius down to the orbital "keel" of the frontal lobe (fig. 4B). By reference to the charts of the cortical areas in Winkler and Potter's classical atlas of the cat's brain, it is evident that these corticipetal fibres from the dorsomedial nucleus are terminally related to areæ prefontalis, orbitalis lateralis, orbitalis intermedia and orbitalis medialis. These areas form component parts of the prefrontal granular cortex.

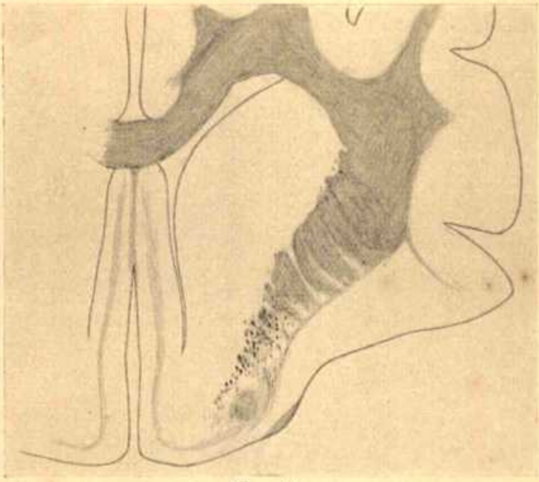

FIG. 4A.

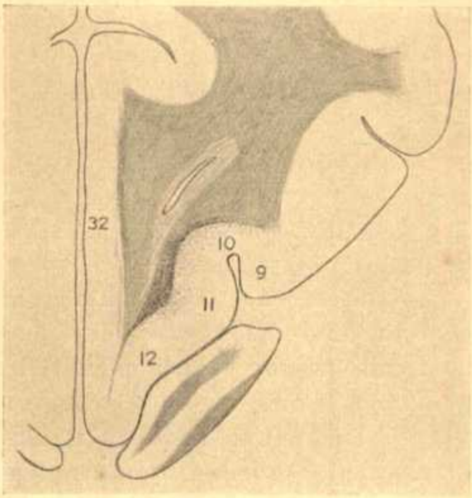

FIG. 4B.

FIG. 4.—A, Section through the rostral part of the septum of Cat 19, showing degenerated fibres in the internal capsule. × 4. B, Section through the frontal pole of the cerebral hemisphere of Cat 19. × 4. The numbers indicate the position of Brodmann's cortical areas.

Besides the degeneration already noted, the fibres of the interanterodorsal commissure (which is involved by the rostral extremity of the lesion in the mid-line) show an abundant deposit of Marchi granules which can be traced up into the anterodorsal nucleus of either side, and there is also Marchi degeneration in the inferior peduncle of the thalamus which results from the injury to the medial olfacto-habenular fibres. No certain evidence was found of degenerated fibres extending from the lesion into the lenticular nucleus.

*Cat* 21.—Operated September 27, killed October 10. The electrode was inserted up to a point 8 mm. anterior to the central point, 1 mm. to the left of the mid-line, and 4 mm. up. A lesion was made by passing a current of 7 milliampères for five minutes.

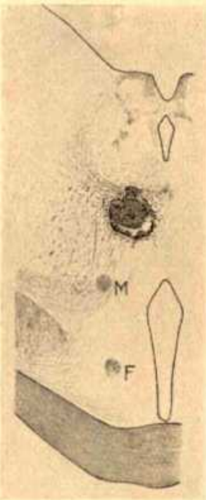

FIG. 5.—Section through the middle of the thalamus of Cat 21, showing the lesion. × 4. F, Fornix. M, Mammillo-thalamic tract.

*Microscopical examination.*—At the caudal margin of the thalamus the lesion lies close to the mid-line on the left side, extending almost from the upper extremity of the fasciculus retroflexus above to the ventral medullary lamina below. At this level it occupies much the same position as the lesion in Cat 7 which is illustrated in fig. 2. Further forwards it is situated rather more ventrally and, in the middle of the thalamus (in sections passing through the optic chiasma, the rostral pole of the lateral geniculate body, and the caudal end of the corpus callosum), it lies up against the mid-line in the most medial part of the ventral region of the thalamus (fig. 5). The lesion is approximately circular in section, measuring 1·5 mm. in diameter. It involves the nucleus centralis medius close to the mid-line and the nucleus submedius, and more caudally the upper end of the fasciculus retroflexus, the nucleus parafascicularis, and the medial part of the centre median nucleus. The dorsomedial nucleus has escaped injury (except, possibly, for its extreme caudal pole). Two sections in front of that shown in fig. 5, the lesion is no longer present.

From the site of the lesion, Marchi degeneration extends into the ventral part of the dorsomedial nucleus, in the periventricular fibres as far up as the habenular ganglion (but not ventrally below the level of the lesion), laterally in the fibres of the commissura media into the nucleus paracentralis and nucleus centralis lateralis of both sides, and slightly in the fibres of the medial medullary lamina. It is also present in the root of the left habenulo-peduncular tract (which is involved by the lesion at the caudal end of the thalamus), and in the fasciculi of the inferior thalamic radiations which course downwards and forwards towards the ventral medullary lamina. The degenerated fibres in the latter fasciculi evidently arise in part from the dorsomedial nucleus, having been intercepted by the lesion on their way down, and, as the sections are traced rostrally, they are observed to pass into the medial end of the zona incerta and so reach the medial margin of the pes pedunculi. A few of them can be followed further forwards in the most medial fasciculi of the internal capsule (lying immediately adjacent to the intermediate root of the olfactory tract) and ultimately into the extreme rostral part of the external capsule, where they disappear in the same region of the cortex into which fibres were traced from the dorsomedial nucleus in Cat 19. The majority of the degenerated fibres which reach the ventral medullary lamina from the lesion run ventrolaterally in amongst the most medial fasciculi of the internal capsule and, having penetrated the latter, turn laterally to reach the globus pallidus, beyond which they could not be traced with certainty. There is no Marchi degeneration in the inferior peduncle of the thalamus.

*Cat* 22.—Operated September 30, killed October 12. The electrode was inserted to reach 8 mm. in front of the central point, 1 mm. to the left of the mid-line, and 4 mm. above the transverse plane. A current of 7 milliampères was passed for five minutes.

*Microscopical examination.*—The track of the needle passes forwards in the mid-line along the cerebral aqueduct, and at this level a slight injury to the ventral fibres of the posterior commissure has given rise to well-marked Marchi degeneration. The main lesion is quite small, measuring 1·7 mm. in transverse and 3 mm. in vertical diameter, and lies in the mid-line close to the dorsal surface of the thalamus. It involves only the nucleus paraventricularis anterior (extending up as far as the ventral margin of the habenular ganglion), the extreme medial margin of the dorsomedial nuclei of both sides, and the nucleus centralis medius.

A fine Marchi deposit is present in the fibres of the commissura media extending laterally on both sides as far as the nucleus centralis lateralis and also in the fibres of the periventricular system immediately adjacent to the lesion. No degenerated fibres extend into the hypothalamus and none reach the internal capsule. There is a slight degree of Marchi degeneration in the most caudal fibres of the inferior thalamic peduncle of the left side.

*Cat* 18.—Operated July 22, killed October 13. Under ether anæsthesia the bone over the right frontal area was removed as far as necessary. The frontal pole of the hemisphere was divided in a transverse plane 1 cm. from the tip with a sharp tenotome. The ensuing hæmorrhage was controlled and the wound sutured. The cat made a good recovery from the operation and exhibited no unusual symptoms.

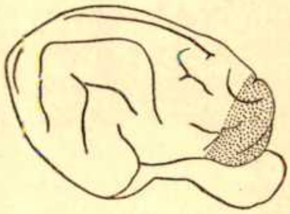

FIG. 6.—Lateral view of the right hemisphere of Cat 18, showing the extent of the frontal cortex whose connections with the thalamus had been severed by the lesion.

The extent of the lesion in the right frontal lobe was studied after death by making sections of the fresh brain and studying them with the aid of a binocular dissecting microscope. The cortical area which had been severed from the rest of the brain by the lesion is indicated by the stippled area in fig. 6. The corpus striatum was not involved by the injury.

*Microscopical examination.*—Complete serial sections were taken through the thalamus and stained with Borell's methylene blue. In the most rostral sections, the course of the degenerated fibres through the anterior thalamic radiations is marked out by blue staining.

The elements of the anterior nucleus and of the lateral nucleus, as well as the nucleus centralis lateralis, nucleus centralis medius, nucleus reuniens, centre median nucleus, nucleus parafascicularis, nucleus submedius and nucleus paratænialis are all normal on the side of the lesion, and stand out in contrast with the atrophic areas in the dorsomedial and ventral nuclei.

In rostral planes, the cells of the lateral third of the dorsomedial nucleus (extending dorsally up to the habenular nucleus) have undergone almost complete atrophy. More caudally, the degeneration is a little more extensive. At its posterior extremity, the nucleus is split into medial and lateral parts by the lateral root of the habenulo-peduncular tract. The cells of the lateral part are atrophied, while those of the medial part are unchanged.

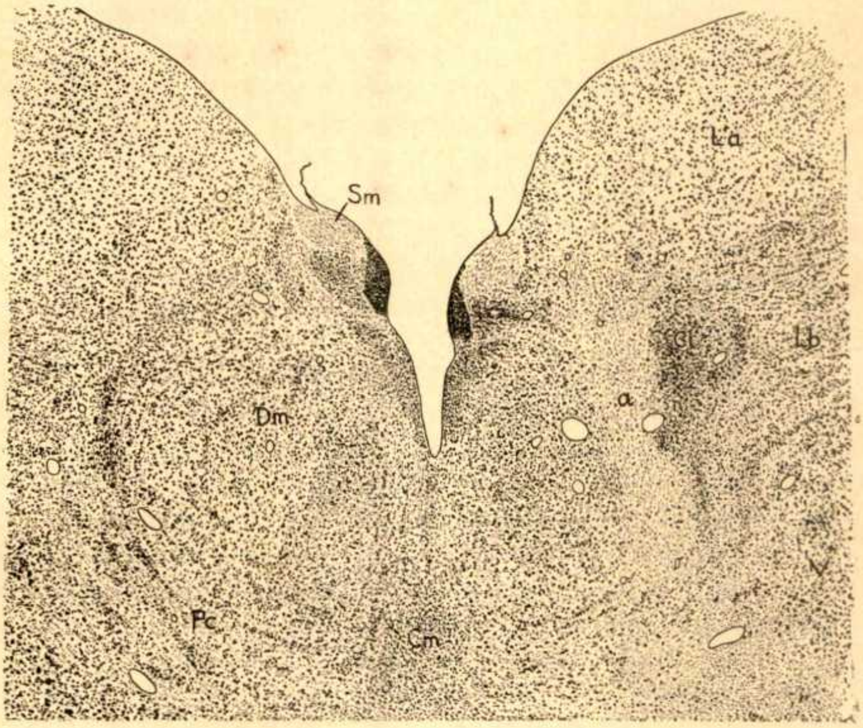

FIG. 7.—Section through the dorsal part of the thalamus of Cat 18, showing the cell atrophy which has followed on a lesion of the frontal cortex. × 20. This figure has been drawn from a section stained with Borell's methylene blue, by means of a projection apparatus. a, Area of cell atrophy in the lateral part of the nucleus dorso-medialis ; Cl, nucleus centralis lateralis ; Cm, nucleus centralis medius ; Dm, nucleus dorso-medialis ; La and Lb, nucleus lateralis ; Pc, nucleus paracentralis ; Sm, stria medullaris ; V, nucleus ventralis, pars arcuata.

Thus, by reference to the cellular atrophy which affects it after an injury to the frontal pole of the hemisphere, the dorsomedial nucleus in the cat may be subdivided into medial and lateral portions. An examination of Nissl preparations of the normal nucleus shows that these two parts can also be differentiated on the basis of cytoarchitecture, the cells of the lateral part (connected with the frontal cortex) being smaller and more fusiform in shape.

Atrophy of cells is also to be found very distinctly in the ventral nucleus. Most rostrally this affects, to a moderate extent, the ventromedial half of the nucleus ventralis, pars anterior. Behind this level the atrophy is mainly confined to the ventral nucleus, pars medialis, which, except at its most anterior part, is almost completely degenerated, very few normal cells remaining. On the other hand the nucleus submedius (? = nucleus medialis ventralis), which lies medial to the mammillothalamic tract, appears normal. At the more anterior levels of the thalamus the pars externa of the ventral nucleus also shows an area of cellular atrophy, but caudally this is only slightly indicated. At caudal levels the cellular degeneration of the ventral nucleus involves the medial part of the pars arcuata, extending out 3·5 mm. from the mid-line. This atrophy shrinks in more posterior sections until it is limited to a small circumscribed patch in the medial " tail " of the arcuate nucleus.

The nucleus paracentralis is normal at rostral levels, but posteriorly many of its cells have undergone complete degeneration, so that the area of cellular atrophy in the medial part of the ventral nucleus becomes here linked up with that in the lateral part of the dorsomedial nucleus. No cellular atrophy is found behind the level of the thalamus.

*Experimental lesions in the rat's brain.*—One of us has already adduced evidence, on the basis of the Marchi method, of a reciprocal fibre connection between the dorsomedial nucleus and the frontal pole of the rat's brain (Clark, 1932 *b*). In the following three experiments on rats, a small lesion was made in the tip of the frontal pole of the left hemisphere with a discission needle. The animals were killed approximately three months later and the extent of the lesion studied in the fresh brain with the aid of a binocular dissecting microscope. A complete set of serial sections through the thalamus was then prepared and stained with Borell's methylene blue.

*Rat FF.* 1.—Examination of the brain after death showed that the lesion had severed the rostral 3 mm. of the frontal pole from the rest of the hemisphere and involved the olfactory peduncle. The microscopical sections show that the anterior end of the striatum was also injured in front of the anterior commissure.

Serial sections through the thalamus demonstrate the following features. On the side of the lesion there is very distinct atrophy (indicated by marked shrinkage and poor staining of the cells) of the lateral third of the dorsomedial nucleus and also of the whole of the nucleus medialis ventralis. On the other hand the nucleus centralis medius, nucleus paracentralis, nucleus centralis lateralis, and more caudally the nucleus parafascicularis and its lateral extension (the homologue of the centre median nucleus) are quite normal in appearance. Similarly, there is no sign of cellular atrophy in the anterior, ventral, lateral, or other thalamic nuclei. The degenerated areas are very clearly defined and stand out in conspicuous contrast with the rest of the thalamus in methylene blue sections.

*Rat FF.* 2.—Examination of the brain after death showed that the lesion had cut transversely across the left frontal pole 4·5 mm. behind its rostral extremity, and had involved the olfactory peduncle and the anterior 1·5 mm. of the striatum (caudate nucleus + putamen).

Serial sections through the thalamus demonstrate an almost complete atrophy on the left side of the lateral two-thirds of the dorsomedial nucleus, of the nucleus anteromedialis, nucleus medialis ventralis, and the left half of the nucleus reuniens. In contrast with these degenerated areas there is no apparent change in the following nuclei: anterodorsal and anteroventral, paratænial, lateral, ventral, paracentral, lateral central, nuclei of the mid-line (except the left half of the nucleus reuniens), parafascicular and centre median.

*Rat FF.* 3.—In this case the lesion was extremely small. Besides injuring the olfactory bulb, it was confined to the extreme tip of the frontal pole, just incising the thickness of the cortex at this point.

Serial sections through the thalamus showed no cellular atrophy in any of its elements.

## DISCUSSION AND SUMMARY.

The discussion of the results of the experiments which have been recorded in this paper may best be accomplished by considering separately the various nuclei involved.

*Nucleus dorsomedialis.*—(Nucleus medialis *a*, nucleus medialis dorsalis of other authors). In Cat 19, the lesion was practically confined to this nucleus and the immediately adjacent mid-line nuclei. Marchi staining showed that, in addition to sending fibres into the medial medullary lamina and the periventricular system, the nucleus emits corticipetal fibres which run ventrally into the most medial fasciculi of the internal capsule, and then pass forwards in close relation to the septum and the basal surface of the brain, to terminate in the granular cortex of the frontal lobe represented by areæ prefrontalis, orbitalis lateralis, intermedia and medialis. Conversely, in Cat 18 and in Rats

FF 1 and FF 2, a very distinct cellular atrophy affecting the lateral part of the dorsomedial nucleus was found after severing the connection between the frontal pole of the hemisphere and the thalamus. It may therefore be concluded that cortical projection fibres from the dorsomedial nucleus are distributed to the prefrontal region of the cortex, and this confirms the results obtained by the Marchi method in the rat's brain (Clark, 1932 *b*). It is relevant to recall that in the higher primates this region of the cortex undergoes a remarkable expansion, and that, coincidently with this, the dorsomedial nucleus in these forms shows a progressive enlargement and a clear differentiation into lateral and medial elements (Friedemann, 1912; Pines, 1927; Clark, 1930). It may be inferred from our experiments that the lateral element is the source of the corticipetal fibres. We believe that the connections of the dorsomedial nucleus with the periventricular system on the one hand, and with the prefrontal region of the cortex on the other, may be of considerable significance. It is evident that the nucleus provides a mechanism through which the cortical levels can be brought into direct functional relation with the activities of the hypothalamus.

*Nucleus submedius.*—This nucleus in the cat's thalamus is probably homologous—at least in part—with the nucleus medialis ventralis of the rat. In Cat 21 the nucleus submedius was destroyed by a small localized lesion. As a result, in addition to a small amount of degeneration in the periventricular system, degenerated fibres were found passing ventrally to the medial part of the internal capsule. A very few were traced forwards to the frontal pole of the hemisphere, but we think it certain that these originate in the dorsomedial nucleus, having been injured by the lesion on their way down past the nucleus submedius. Most of the degenerated fibres, which evidently have their origin in the submedial nucleus, penetrate the internal capsule to reach the lenticular nucleus. This connection corresponds precisely with that of the nucleus medialis ventralis in the rat's brain as demonstrated by the Marchi method (Clark, 1932 *b*). A marked atrophy of the whole of this nucleus was found in Rats FF 1 and FF 2, following a lesion in the frontal pole of the hemisphere, and the significance of this requires further investigation. In both these cases, however, the rostral part of the striatum (caudate nucleus + putamen) had been involved by the injury. This fact, together with the absence of positive evidence based on Marchi degeneration, precludes the assumption of a direct cortical connection of the nucleus medialis ventralis.

*Nucleus anteromedialis.*—In one experiment (Cat 6) this nucleus was involved by the lesion, but only to a very slight extent at its medial margin. In Rat FF 2, the whole nucleus had undergone atrophy following a lesion of the frontal pole of the hemisphere. As in the case of the nucleus medialis ventralis, further experimental inquiry is needed to elucidate the meaning of this degeneration (e.g., whether it is secondary to an injury of the cortex involving that part of the area cingularis which extends on to the medial surface of the frontal lobe, or whether it is associated with the injury of the rostral end of the striatum). In this experiment on the rat, the sharp contrast between the degenerated anteromedial nucleus and the unaffected anteroventral nucleus may be noted, for it serves to emphasize the distinction between these two elements which is apparent in their normal cytological features.

*Nucleus centralis lateralis.*—This nucleus remained unaffected by lesions of the frontal pole of the hemisphere. Marchi sections indicate that it is closely related to the commissural fibres of the thalamus which run through the nucleus centralis medius, and that, by way of its fibre connections with the latter nucleus, it may also serve as a link through which the more laterally situated nuclei of the thalamus are brought into relation with the mid-line nuclei and the periventricular system of fibres.

*Centre median nucleus.*—This nucleus was partly destroyed in Cat 7. No degenerated fibres were traced from the site of lesion beyond the immediately adjacent thalamic nuclei (except in the habenulo-peduncular tract which was also injured in this experiment). This result is in accord with the experiment recorded elsewhere in which the centre median nucleus was also injured (Clark and Boggon, 1933). It may also be noted that lesions in the frontal pole of the hemisphere led to no atrophy in the nucleus. Thus it appears that the centre median nucleus is an intrathalamic mechanism concerned rather with the linking up of other thalamic elements, a conclusion reached by one of us on the basis of comparative anatomical studies (Clark, 1932 *a*).

*Nuclei of the mid-line.*—Following lesions limited practically to the mid-line nuclei (nucleus paraventricularis anterior, nucleus commissuralis interanteroventralis, nucleus commissuralis interanterodorsalis, nucleus centralis medius), degeneration was limited to commissural fibres and periventricular fibres. The former could be traced out either to the anterodorsal nucleus, or through the nucleus paracentralis as far as the nucleus centralis lateralis. They could not with certainty be followed further. The degenerated periventricular fibres were followed up dorsally into the paratænial nucleus and the dorsomedial nucleus.

Ventrally they could be traced in a subependymal position as far as the junction of the thalamus proper with the hypothalamus, but in no case actually into the substance of the hypothalamus. Rioch (1931) has demonstrated with Weigert material a fibre connection between the mid-line nuclei of the thalamus and the hypothalamic nuclei. From our experiments, it appears certain that (so far as myelinated fibres are concerned) this connection is established by short relays of neurones.

*Thalamo-cortical projection fibres.*—The positive evidence which we have adduced of cortical connections of the dorsomedial nucleus and, in a previous communication, of the anterior nucleus (Clark and Boggon, 1933), indicates that, at least in lower mammals, the prefrontal cortex and the cortex of the gyrus cinguli must be included among the thalamocortical projection zones (in addition to the somato-sensory, visual and auditory areas). This result finds no support in the conclusions attained by Poliak in his recent elaborate monograph on the afferent fibre systems of the cerebral cortex in primates (1932). It should however be noted that: (1) this author did find Marchi degeneration in the gyrus cinguli along the dorsal surface of the corpus callosum in one of his experiments (No. 2) after a lesion involving the anterior limb of the internal capsule, but he does not appear to consider the question of this degeneration being the result of an interruption of thalamo-cortical fibres; (2) in none of his experimental lesions were the fibres of the anterior thalamic radiations, which course forwards close to the basal surface of the brain and which (in the cat and the rat) contain the projection fibres from the dorsomedial nucleus, interrupted by the injury.

We are much indebted to the British Association for the loan of the Clarke-Horsley stereotaxic instrument which we used in the course of the experiments recorded in this paper.

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# ON A CORTICAL FLEXOR TONE IN THE FORE-LIMB OF THE CAT, WITH OBSERVATIONS ON THE HEMIPLEGIC ATTITUDE IN MAN.

BY D. M. BLAIR AND R. J. S. McDOWALL.

*(From the Departments of Anatomy and Physiology, King's College, London.)*

VARIOUS clinical conditions in man associated with tonic spasm have been studied from time to time in relation to the classical picture of experimental decerebrate rigidity in animals. In particular, attempts have been made to relate the postural effects seen in clinical cases of hemiplegia and paraplegia to the position assumed in animal decerebrate rigidity; and in comparing and contrasting the human and animal pictures attention has been drawn to one striking difference, that while in the animal the fore-limb shares with the hind-limb a position of rigid extension, in man the arm is usually in a position of rigid flexion and adduction. Recent papers by Manson and Ferguson (1930) and by Brain (1927), for example, emphasize this difference and contain brief reviews of earlier discussions of the clinical counterpart of animal decerebrate rigidity.

The following observations seem to have a direct bearing on this problem of difference. They are put forward with all due reserve in that they are observations made on animals under general anæsthesia. But it may be claimed with some justice that phenomena seen under successive stages of general anæsthesia are not unconnected with the effects produced by experimental or pathological lesions of the brain. For, in general, the successive stages of anæsthesia reflect effects on successive brain levels. And, as will be seen, our observations are supported by experimental results and throw a suggestive light on pathological conditions. Careful observation of the behaviour of both animals and man under anæsthesia is indeed likely to provide a fruitful field for investigation of cerebral function.

In cats under avertin anæsthesia we have repeatedly noted a stage at which the hind-limbs are rigidly extended while the fore-limbs are rigidly flexed and adducted. As anæsthesia deepens beyond this stage, a position is assumed of extensor rigidity in all limbs, which is succeeded in turn by a stage of complete relaxation of all limbs comparable to what is termed "surgical anæsthesia" in human operative practice. These stages have been observed to occur in reverse order when an animal is recovering from deeper anæsthesia. The stage of flexed adducted fore-limbs with extended hind-limbs has been noted most regularly when avertin has been given intravenously during preliminary ether anæsthesia. In one consecutive series of eight cats anæsthetized in this way the stage was seen distinctly in six, indefinitely in one, and not at all in another. In the last case a considerable amount of ether was given before giving avertin. This particular stage has been observed much more irregularly when ether alone, or avertin alone, was employed.

At the stage referred to, the animal is completely unconscious; while recovering from it no signs of struggling are seen until a much lighter stage of anæsthesia is reached. The position of the limbs is entirely unchanged by altering the position of the animal as a whole, or of its head and neck in relation to its trunk.

As this position preceded, in deepening anæsthesia, the stage of quadrupedal extension resembling the attitude of decerebrate rigidity, it seemed likely that it was related to supra-mesencephalic function. We therefore investigated the effect on this posture of removal of cerebral cortex. It was found that a suitable removal of cortex on one side caused the flexion in the opposite fore-limb to be replaced by extension. It was more difficult to observe on the trephined animal the typical stage of rigidly flexed fore-limbs and rigidly extended hind-limbs, because the deep anæsthesia induced before trephining was not always promptly recovered from. The amount of avertin by then given in some cases was apt to induce a delayed effect going on to the production of complete muscular relaxation, lasting, it might be, for many hours. The blood-pressure in such cases remained normal, so that this condition was not one of surgical shock, but rather an intense "sleep" condition, such as has been known to occur at times in the clinical use of avertin. But, nevertheless, in some animals we were able to observe, after trephining, the position with rigidly flexed fore-limbs and rigidly extended hind-limbs; unilateral removal of cortex was then followed by extensor rigidity in the opposite fore-limb. In some other cases where, after trephining, both fore-limbs persisted in a condition of only slight rigidity and partial flexion, and on removal of cortex on one side little or no change in the attitude of the limbs took place, the fore-limb on the side of cortical removal was found to resist passive extension slightly or even to respond with a definite flexor pull, while the fore-limb, the cortical connections of which had been interfered with, now showed no such signs of flexor tone.

Thus we found that this tonic flexor position of the fore-limb which is "released" at a certain stage of anæsthesia, is abolished by contralateral removal of cerebral cortex, just as we had previously noted that it disappeared with deepening anæsthesia. It therefore seems to be maintained by cortical influence.

An attempt was made to determine more precisely whether the maintenance of this flexor tone was associated with any particular area or extent of cortex upon ablation of which the flexor tone disappeared. Removal of cortex was done on one side only, also first on one side and then on the other side. Always purely contralateral effects were noted. The motor area was identified by electrical stimulation. Suitable precautions were taken to prevent drying of exposed cortex.

When removal of cortex was strictly confined to the motor area, no alteration in the incidence of this fore-limb flexor tone was observed to follow. Nor was any change seen when cortex was removed behind the motor area, on the lateral aspect of the hemisphere, and the motor area was left intact. But removal of the motor area plus an extent of cortex posterior to it rather greater in size than the motor area itself brought about a loss of flexor tone previously present in the opposite fore-limb, or caused a more definite condition of rigid flexion and adduction previously present to be replaced by rigid extension.

Removal of cortex anterior to the motor area produced no appreciable result until part at least of the motor area also was removed; then the most striking result was increased extensor rigidity of both fore-limb and hind-limb on the opposite side, as has already been described by Warner and Olmstead (1923) to take place on extirpation of the frontal cortex. These authors do not mention any difference of effect in the fore- and hind-limb; we observed that while stimulation of the cut surface of the frontal region diminished distinctly the rigidity of the contralateral hind-limb, a slight flexor tone appeared in the contralateral fore-limb.

According to our observations, therefore, the maintenance of the flexor tone in the fore-limbs does not seem to be localized in any particular part of the cortex by itself. The parietal area seems to be specially concerned, but a fairly extensive ablation of cortex in this region does not bring about loss of the flexor-tone unless the motor area also is destroyed. Removal of the motor area alone does not affect the flexor tone, but we have never seen this tone disappear upon removal of any other area of cortex while the motor area remained intact. Loss of the flexor tone seems to follow upon cutting off the motor area plus a considerable extent of adjoining cortex.

How far this flexor rigidity which we have studied in the fore-limb of the cat corresponds to the clinical flexor rigidity of the arm in man can be at present a matter for conjecture only. Rigid flexion of the arms and extension of the legs is often seen in early stages of general anæsthesia in man. Sherrington has stated, in a personal communication referred to by Brain (1927), that in monkeys prior to deep anæsthesia, there is frequently a long-maintained flexor position of the fore-limbs. It may quite well be the case that in man, owing to the high degree of integration throughout the cerebral cortex, cutting off a localized part of the cortex by a pathological lesion (as the motor area in hemiplegia) may so interfere with cortical function as a whole as to "release" a flexor tone in the arm, just as is done in incomplete anæsthesia. We have demonstrated that in the cat a cortical fore-limb flexor tone can persist after ablation of the motor area. May it be that the extensor rigidity of the arms, more rarely seen in patients with cerebral lesions, indicates a more extensive removal of cortical control than that of the motor area only, as is the case in the cat?

But the main significance of our present observations, in relation to the problem of flexor rigidity of the arm in man, is the demonstration that in the cat extensor rigidity of the hind-limbs may co-exist with either extensor *or* flexor rigidity of the fore-limbs, under different conditions. It is therefore unnecessary to force a strict comparison between the complete "decerebrate rigidity" posture in animals, and the human clinical posture of flexed arms with extended legs. If flexor rigidity and extensor rigidity are both found in the fore-limbs in animals, it is beside the point to compare the human flexor position with the animal extensor position only, and to seek an explanation of the difference in posture in the altered normal use of the fore-limbs in man.

Brain (1927) has suggested that the hemiplegic position with flexed arm and extended leg represents a "release" of the primitive anthropoid erect attitude. But it is surely unsound to argue that pathological interference with normal function of the human brain may "release" an atavistic attitude which in a lower animal is the outcome of the activity of a normally acting brain—to argue in other words, that a localized pathological lesion has the effect of putting back the hands of the evolutionary clock. The work of Richter and Bartemeier (1926) is a striking demonstration against this argument: they showed that the decerebrate attitude in sloths reproduces in detail the upside-down hanging posture peculiarly characteristic of these animals themselves. Brain's demonstration that, when the body of a hemiplegic patient is brought into the quadrupedal-standing position, the flexed arm then becomes extended, is merely a demonstration of the activity of proprioceptive and labyrinthine reflexes, which he admits must be brought into play in order to produce this phenomenon (extension of the arm does not follow mere passive flexion of the leg upon the trunk).

Our investigation lends some support to the suggestion of Kinnier Wilson (1920) that the flexed arm position in man is an incomplete form of the decerebrate posture in animals. On the basis of our observations in the cat, we would put it that the flexor position of the arm is the result of incomplete decerebration and depends on some remaining cortical influence.

## SUMMARY.

(1) A fore-limb flexor position seen in cats under avertin anæsthesia is described.

(2) Evidence is given of the cortical nature of this flexor tone.

(3) The bearing of these observations on the human hemiplegic posture is discussed.

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## NOTICES OF RECENT PUBLICATIONS.

*The Sign of Babinski.* A Study of Cortical Dominance in Primates. By J. F. FULTON and A. D. KELLER. London: Baillière, Tindall and Cox. 1932. Pp. 165. Price 31s.

Physiological analysis of the Babinski response has shown it to be but an integral part of a flexion reflex of the human lower limb, which in turn represents the nociceptive flexion reflex of the decerebrate and spinal cat described by Sherrington. However, the identification has lacked completeness, since no very definite dorsiflexion of the digits seems to occur in this reflex as seen in these animal preparations.

The investigations so fully set forth in this monograph have attempted to fill this gap by a series of comparative studies of the normal and pathological plantar responses in primates. For this purpose the authors have had at their disposal a continuously ascending series of animals: macacus, baboon, gibbon and chimpanzee.

In macacus they have performed spinal cord transection and hemisection, and ablation of one or both cortical "leg areas." In the other members of the series, with the single exception of a spinal cord transection in a chimpanzee, they have confined their experiments to cortical ablations.

In all their animals in a normal state, the plantar response was found to be either absent or of the human flexor type. No dorsiflexion response of the hallux was observed. After spinal cord transection in *macacus*, the only plantar response seen was plantar flexion of the four lateral toes, but thoracic hemisection of the cord was followed by the appearance of a homolateral Babinski plantar response. Ablation of the cortical representation of the leg failed to effect a change in the normal plantar response. Similar results were obtained in the *baboon*, with the exception that ablation of the cortical "leg area" was followed on plantar stimulation by dorsiflexion and fanning of the four lateral toes, the hallux remaining inactive.

In a *gibbon*, ablation of one cortical "leg area" was followed by the appearance on stimulation of a typical Babinski response in the contralateral foot. In the *chimpanzee*, ablation of the "leg area" is followed by the appearance of a Babinski response, which consists of dorsiflexion of the four lateral toes, dorsiflexion and marked abduction of the hallux, and finally fanning and lateral deviation of the four lateral toes. Associated limb flexion is present in the earlier stages, but tends to diminish and to disappear after some weeks. The focus of the receptive field seems to be the skin of the plantar surface of the toes, but the whole surface of the foot may be effective in favourable cases. The adequate stimulus is pinching and pricking of the skin and pressure over the region of the malleoli.

In addition to their observations on this reflex, the authors found that as the animal scale is ascended, the degree of paralysis of the affected leg after cortical ablation increases, and the extent of restoration of power diminished. Thus the dog can walk a few hours after ablation of its motor cortex, but in the chimpanzee there is profound paralysis of the affected leg and slow and imperfect recovery. This they attribute to increasing cortical dominance in the higher animals.

The authors have been fortunate in their opportunity to study this series of primates in this way, which made it possible for them to subject the flexion reflex and its digital components, and also the associated crossed plantar response, to a careful analysis. More might have been made of this opportunity. Thus, they might have mapped out the receptive field, as it has been mapped in the cat and in the human subject; they could have determined the rôle played by stimulation of deep structures, the range of adequate stimuli and the full field of motor response.

With the results actually obtained, it is reasonable for the clinical neurologist to feel some disappointment. By adopting an unsound clinical basis of study, namely, by studying the reflex in terms of Oppenheim's, Gordon's and Chaddock's signs, the study of the receptive field and of the stimulus have been confused, and from the medley of observations obtained no determination of receptive field or of range of stimuli has been possible. The limb flexion component of the response has not been adequately studied and the crossed plantar response has escaped investigation altogether. In the case of the apes we still lack, therefore, that finished analysis of the flexion reflex and its associated plantar response that we have long possessed in the case of animals so widely separated as the cat and man.

The clinician will be struck by the statement in the opening pages of the monograph that no previous physiological analysis of the Babinski response has been attempted. It appears, however, that the authors intend to convey something wholly different; namely, that no previous experimental study of the response in apes has been attempted. After all, the analysis of a reflex reaction occurring in man can be made only by the study of man, and the investigation of a simian reflex—however precise the experimental method of study—can do no more than throw light upon what happens in the ape.

Actually, human physiological studies of the Babinski response have been made and the references thereto may be found in the author's bibliography. The monograph contains a wealth of precise experimental detail and numerous illustrations mostly bearing upon points of technique. These will be of value to workers engaged in this field, and it is probably for them that the book will have its chief interest and importance.

*Atlas Anatomicum Cerebri Humani.* By G. JELGERSMA. Scheltema and Holkema's Boekhandel en Uitgevers Mij. N.V. Amsterdam. 1932.

This atlas consists of 108 loose plates, 43 by 32 cm. in size, of photographs of 168 sections of the human brain and spinal cord stained by the Weigert-Pal method. The first 67 are in the coronal plane, then come 7 of sagittal sections and the remaining 31 show sections in the horizontal plane. The last three plates are of horizontal sections of each segment of the spinal cord. These are the least satisfactory part of the atlas, and compare unfavourably with Bruce's atlas of the spinal cord. The sections photographed are not always truly representative of the segment. For example, C 5 has as narrow a ventral horn as C4, and D12 as D11. The sections, that is to say, are taken through the uppermost end of each segment and not through its centre. Further, the characteristic appearances of the first three sacral segments are not illustrated, only two sacral sections from low in the conus being reproduced. Apart from these three plates the illustrations are excellent and are of great value both for teaching and research. The technical skill both of the histological preparations and of their reproduction by helio is of a high order.

No descriptive text, apart from a short note on the technique employed, has so far been published with the atlas.

*Die Multiple Sklerose Einst und Jetz.* Von R. BING. S. 41. Basel: Benno Schwabe. 1932. Price 2 fr. (Swiss).

This reprint from the *Schweizerische Medizinische Wochenschrift* of a lecture on the nature and pathogenesis of Disseminated Sclerosis will prove useful to those unable to study the enormous literature on this disease. The author reviews shortly its history and the many conceptions of its pathology put forward by earlier and recent writers; he accepts, as most authorities do now, the view that the lesions are primarily inflammatory and the result of some exogenous cause, as an infection, but he emphasizes the part possibly played by endogenous factors. The most important contribution to our knowledge which Bing presents is the result of the careful investigation undertaken by the Public Health Authorities and the Swiss Neurological Society on the distribution of the disease in Switzerland; this brings out many facts on the possible influence of climate, altitude, occupation and social standing, as well as on the age of onset and familial incidence, which cannot be neglected in any future study of the disease.

*Syndromes acromégaliques au Cours de Tumeurs intracraniennes non hypophysaires.* Par P. PUECH. Pp. 39. Paris: C. Serre. 1933.

Two cases of meningiomas of the lesser wing of the sphenoid are described in patients with symptoms of acromegaly, but it must be admitted that in neither were the latter pronounced. The patients died after operations and in

JULY, 1933.

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BRAIN.

PART 2, VOL. 56.

# SOME OBSERVATIONS ON THE FIFTH AND SEVENTH CRANIAL NERVES.

BY E. ARNOLD CARMICHAEL,[1]
*Research Unit, National Hospital, Queen Square, London,*

AND

H. H. WOOLLARD,
*Department of Anatomy, St. Bartholomew's Hospital Medical School, London.*

THE present inquiry was begun because Dr. Hinds Howell placed at our disposal a number of cases of trigeminal neuralgia which he had treated by alcoholic injection of the Gasserian ganglion. A study of such cases, it was thought, would enable us to compare the anatomical and physiological results of this form of treatment with that of surgical removal of the Gasserian ganglion.

It is unnecessary to re-state the clinical position in regard to the injection or the surgical methods of treatment, but we wish to present evidence in what follows for asserting that the whole Gasserian ganglion can be permanently destroyed by an injection of alcohol. Further, it was hoped that in the course of such a study we might investigate once more the many problems appertaining to the cranial nerves still left unsolved, despite the many excellent and thorough investigations already published. Some of the problems that interested us were the anatomy of the taste nerves, the anatomy and physiology of deep pressure-pain, the course and distribution of the proprioceptive fibres in the ocular and facial muscles and with this, the problem as to whether such fibres can give rise to the sensation of pain, and the existence of accessory pathways for pain.

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[1] This article formed the basis of one of the Oliver-Sharpey Lectures at the Royal College of Physicians, London, 1933.

## General Remarks on the Fifth Nerve.

At the outset we offer a few observations on the general biological position of the fifth nerve in order to obtain some perspective of the nature and quality of the cranial nerves.

In a relative sense the anatomy and physiology of the fifth nerve are well known. The gradual evolution of the nerve through the representatives of all the main classes of vertebrates has been traced. Such studies have made it clear that the nerve is of a two-fold nature, the ophthalmicus being one part and the maxillo-mandibularis the other. Kappers [22] has identified these two nerves in amphioxus where they are quite separate. In the cyclostomes (Johnston [20]), the next lowest vertebrates after amphioxus, the two nerves have fused and a descending intra-medullary tract belonging to the ophthalmicus is present in the brain-stem. It is doubtful, however, if an ascending mesencephalic root exists. In all higher forms the ascending mesencephalic root and the descending root are present and, when we reach the reptiles, the nerve is morphologically complete. The mesencephalic root in these extends cranially into the tectum, and a principal nucleus is present which gives crossed fibres to the mesial fillet as well as a descending root contributing crossed fibres to the spinothalamic tract. In all classes of vertebrates the ophthalmicus is the main constituent of the descending root; it runs ventral to the maxillo-mandibularis portion of the root and reaches further caudally than these. This descending root of the ophthalmicus comes into association with motor centres of the spinal cord, as those for the pectoral fins in fishes, those for the fore-limbs in the amphibia, in the frog it even reaches the lumbar enlargement, and those for the cervical muscles in man. The maxillo-mandibularis portion is connected more closely to the branchial system of nerves and the connections of its descending roots are intimate with the seventh, ninth and tenth cranial nerves.

Comparative anatomy indicates that the functions of crude sensation of the nerve precede those of a discriminating quality, the latter not appearing until the reptiles are reached (Brouwer [5], Johnston [19], Herrick [18], Woollard [32] *et alia*). When the nerve can first be identified it is the great somatic sensory nerve of the head region. The ophthalmicus innervates the post-axial region of the head, i.e., the dorsum, starting from the tip of the nose, which is the true front end of the body, while the maxillo-mandibularis functions as the somatic sensory component for all the remaining cranial nerves which contain no such fibres except the vestiges of those formerly innervating the lateral line system. This lateral line system, which subserves a variety of tactile sense by means of which the swimming animal became aware of the swish of the water along its body, disappeared when vertebrates became terrestrial and the remains of the nerves belonging to it became clustered around the external auditory meatus as the auricular nerve of Arnold, this being made up of small fasciculi from the seventh, ninth and tenth cranial nerves.

The fact that the fifth contributes to the innervation of the mouth might suggest that its range is not confined to cutaneous areas. The vertebrate mouth is, however, a new formation and the fifth becomes involved in it secondarily while still keeping its cutaneous quality. On phylogenetic grounds it is improbable that the fifth should carry impulses subserving taste.

The opthalmicus is then a purely cutaneous nerve with its own history and running its own course in the development of each vertebrate. In human development it runs in the mesenchyme that invests the head, viz., the paraxial mesoderm, and centrally it gives off the long descending tract ultimately connected with the spinal motor centres. It is thus the basis of protective reflexes, made more important by the fact that it is the front nerve of the body. The maxillo-mandibularis is related to the first branchial arch and the nerve is embedded in the mesenchyme of the arch, thus differing from the ophthalmicus. Its descending root is, as is to be expected, more intimately related to the other branchial nerves, and it is with the seventh, ninth and tenth that it establishes its medullary connections.

It is to be remembered that the cranial nerves are not modified spinal nerves, but a system which is much older and simpler than these. It is now agreed that the fundamental divisions of the body determined on comparative embryological grounds by Brachet [4] are well founded. The first and oldest portion of the body is the region of the fore-brain vesicle with the olfactory and optic systems and the front end of the pharynx with adjacent structures. It is for this region that the opthalmicus becomes the somatic sensory receptor beginning, and indeed continuing, for the most part to act as the nerve for sensations of a crude quality. The second oldest part of the body is the region corresponding to the brain-stem between the fifth and tenth nerves, and including the branchial apparatus. Here the cranial nerves proper are situated. It is a region where segmentation is transient, doubtful and obscure. The remaining portion of the body, the trunk and the tail with the organs of locomotion and the genito-urinary structures, appears last; it is characterized by a high degree of segmentation, no special sense organs are developed in it and the spinal nerves become aggregated into bundles containing all the afferent and efferent fibres of each segment. The cranial nerves, on the contrary, are more primitive and do not show this combination of all the components, for the ventral and dorsal roots remain separate. The dorsal roots are for the most part mixed nerves but, nevertheless, the older cranial nerves tend to confine each function to different nerves. They must be studied as a special class by themselves, and for the reasons just given they might be expected to offer greater opportunity for unravelling the functions of the peripheral nervous system. The tendency for the cranial nerves, as the fifth, to form descending roots, also distinguishes them. It is in strong contrast with the spinal nerves, and even if neurobiotaxis be the explanation it can still be emphasized as a special character of nerves in the region of the brain-stem.

The mesencephalic root of the fifth is another case of functional segregation in the cranial nerve region (Johnston [21]). Every muscle has its sensory innervation, and it seems definite from experimental investigation (Allen [1]) that the mesencephalic root contains cells the axones of which pass out in the sensory root of the fifth and then traversing the ganglion, but not using its cells, enter the mandibular branch to reach the muscles of mastication. Evidence has been brought forward that this mesencephalic root may be the source of proprioceptive fibres for the masticatory muscles, and perhaps for the ocular muscles (Woollard [31]). The cranial extension of this nucleus, its advance in the mid-brain even to the level of the posterior commissure in man and its proximity to the ocular nuclei, are in accord with such probabilities.

The inclusion of the mesencephalic root in the brain-stem is unexpected, for cells elsewhere performing a similar function are lodged in the dorsal root ganglia. The neural crest from which the Gasserian ganglion is derived is formed at the level of the mid-brain and from the most anterior of the neuromeres of the hind-brain (Van Wijhe [29], Bartlemez and Evans [2]). It may be supposed that the more anterior part of the neural crest, instead of advancing laterally, becomes incorporated in the brain-stem. This incorporation may be in some way concerned with the fact that the mesencephalon is at the junction of anterior and middle constituents of the body as described previously. It has also been suggested that the mesencephalic nucleus is homologous with the large sensory cells which in lower vertebrates lie within the central nervous system and send axones to the muscles and skin. For neither of these hypotheses is there any adequate proof at the moment.

*Material.*—We had twenty cases of trigeminal neuralgia at our disposal; in all but two, who had the ganglion removed by open dissection ten or more years previously, an alcoholic injection of the Gasserian ganglion had been performed by Dr. Hinds Howell. In several instances we had the opportunity of examining the patients both before and after the injection. Twelve cases of facial palsy, due to lesions at various levels of the nerve, and five cases in which the cervical sympathetic had been removed or injured on one or both sides were included in the investigation.

*The Extent of the anæsthesia.*—There is no need to dwell at length on the area from which sensation disappears after destruction of the Gasserian ganglion. Such studies have been published many times and the results of various methods compared—Bolk [3] by the method of dissection, Davies [8] and Cushing [7] after removal of the ganglion, Harris [17] after alcoholic injection. The results obtained by these various methods agree closely. We have found that in the complete cases, ten of the eighteen, investigated by us after alcohol injection the area of anæsthesia resembled in every detail that which follows surgical removal (figs. 1, 2 and 3). The backward prolongation to the ear with the inclusion of the anterior and superior walls of the external auditory meatus and the tympanic membrane may be noted. The area in front of the angle of the jaw is excluded and the line of the anæsthesia drops near the angle of the mouth to the lower border of the ramus of the jaw. In the mouth all the hard and soft palate and the upper half of the anterior pillar of the fauces are included. On the tongue the anæsthesia ceases in front of the vallate papillæ, these falling within the area of the glossopharyngeal nerve.

Like Davies and Cushing we have found that the anæsthesia is often coincident for all forms of sensation, but when such is not the case the tactile loss has usually been the most extensive. We have had little opportunity of studying the recession of the anæsthesia that Davies commented on. In those of our series in whom the ganglia had been destroyed for the longest periods the area of anæsthesia was in no way less than those in whom the ganglion had but recently been injected. In ten of the eighteen cases injected with alcohol there was a complete loss of all forms of cutaneous sensation over the distribution of the fifth nerve. The longest period since the injection was ten years, the shortest a few weeks, and in all the relief from pain was complete. We feel that the examination of these cases favours the view that by means of alcoholic injection the relief from pain is equal to, and the area of anæsthesia is as complete, as that following surgical treatment.

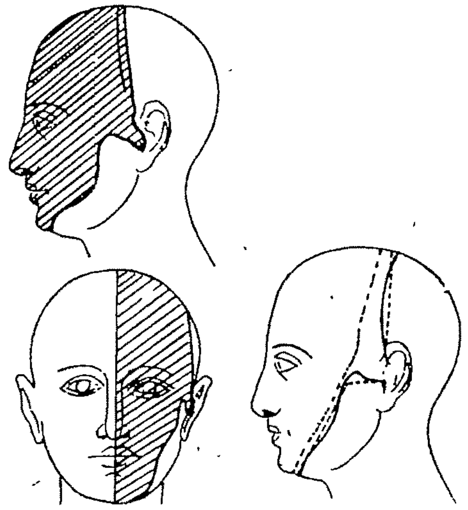

FIG. 1.—Area of anæsthesia after surgical removal of Gasserian ganglion. (Cushing.)

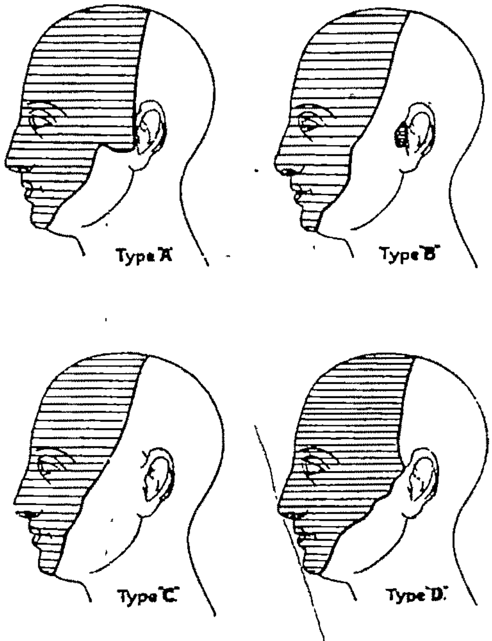

FIG. 2.—Area of anæsthesia after surgical removal of Gasserian ganglion. (Davies.)

*Referred pain.*—There is evidence that headaches may arise through stimulation of the nerve endings in the dura mater; the precise nature of the stimulus is uncertain (Pickering and Hess [25]). The dura of the anterior and middle cranial fossæ, together with the tentorium cerebelli, receive their innervation from the fifth nerve and particularly from the ophthalmic branch. We asked particularly many patients about the occurrence of headache and from some we got the emphatic assertion that they did suffer from headaches on the anæsthetic side. Records as to headache were made in 12 cases: 7 never had any headache, 1 case suffered with headache only on the non-anæsthetic side, while 4 patients were definite that their headaches were felt on both sides of the head. In 2 of these 4 cases the cutaneous area of anæsthesia was complete, but incomplete in the other 2. This suggests that all headaches may not arise through the dural nerves and that headache may arise centrally and be referred to the peripheral distribution of the fifth.

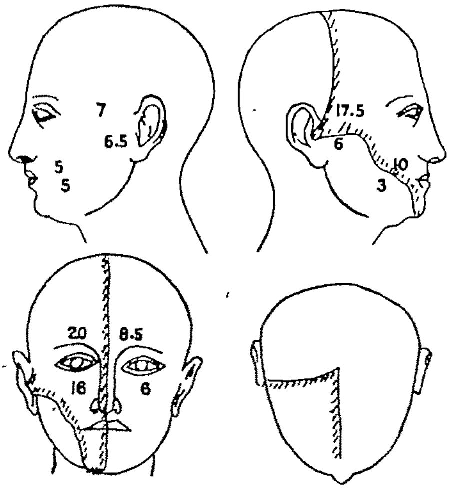

FIG. 3.—Area of anæsthesia after alcoholic injection of the ganglion by Hinds Howell. Algometric readings are indicated.

*Pain reflexes.*—The conjunctival reflex is, of course, abolished and the oculo-cardiac reflex, we believe, is absent too. In testing this reflex upon ourselves we found that it was elicited by a degree of pressure on the globe of the eye which was painful, and not until pain was experienced were we able to detect in polygraph tracings any slowing of the heart. We were reluctant to exert this amount of pressure upon the patients investigated, but we came to the conclusion that ocular pressure pain was absent in those who had been deprived of the Gasserian ganglion, In the five cases examined we were unable to obtain the oculo-cardiac reflex from the anæsthetic side; in two of these cases the anæsthesia was on the left side, in the remainder on the right. All the evidence indicates that pain is the only common sensation in the eye-ball. The optic nerve subserves its special function only, the ophthalmic is the afferent limb of protective reflex arcs aroused solely by pain, while the autonomic nerves regulate the amount of light entering the eye by alterations of the size of the pupil.

*Taste.*—We have taken the occasion to observe the effect of these injections on taste and have met with the same discrepancies which have vexed all other observers. The published investigations show that in about half the cases the taste is unimpaired and in about half it is lost. The reasons put forward to explain the loss of taste have been for the most part anatomical. Thus it has been suggested that the ninth nerve was the sole nerve of taste; that taste first travelled peripherally in the chorda tympani and from there was transmitted through the small superficial petrosal nerve and otic ganglion to the mandibular nerve; that taste impulses were transmitted from the chorda tympani through the great superficial petrosal and spheno-palatine ganglion to the maxillary division of the fifth; that taste travelled back through the chorda tympani and small superficial petrosal and thence to Jacobsen's nerve and the glossopharyngeal and so centrally. These anatomical explanations have always seemed improbable: the chorda tympani and pars intermedia is the most obvious route, though this route does not account for the large number of cases in which taste appeared to be impaired following destruction of the Gasserian ganglion. To account for these Dixon [11] brought forward evidence that the extirpation of the ganglion might readily be accompanied by injury to the seventh nerve, by way of the hiatus Fallopii. We repeated the experiment of injecting the ganglion in the cadaver by means of coloured gelatine solutions in order to find where such injections would most readily spread (fig. 4). This showed that injected material spread along the central root of the fifth into the posterior fossa, over the cerebellar hemisphere and through the hiatus Fallopii to the position of the geniculate ganglion. Dixon's suggestion is therefore not improbable, but in all our cases careful note was made of the condition of the seventh nerve and no impairment of its function was ever discovered in those where taste was absent. It may be that the cells of the geniculate ganglion are more readily affected by the alcohol than the motor fibres of the seventh, though we know of no evidence that this is so.

In our series of seventeen cases in which it was possible to test taste satisfactorily by applying test substances to the protruded tongue, ten had a complete loss on the anæsthetic side, taste being preserved on the normal side. Evidence of loss was accepted only when the substance had been applied for not less than thirty seconds and then did not produce a sensation. In several of these ten cases the injection had been performed over a year previous to the time of testing. Seven cases retained the sensation of taste. We can offer no satisfactory explanation as to why taste should sometimes persist and sometimes be lost after destruction of the Gasserian ganglion. It cannot be explained by the well-known variability of gustatory acuity of the anterior two-thirds of the tongue, since in our cases in which taste was lost on the one side, it was present on the opposite side. Leakage of the injected solution towards the geniculate ganglion undoubtedly does occur; and this explanation of the loss of taste would be satisfactory if one could have detected other evidence indicating impairment of the seventh nerve. In the cases of facial palsy we examined, taste was lost in some and present in others, but most of the cases had peripheral lesions and therefore involvement or escape of the chorda tympani would explain this variation. In three

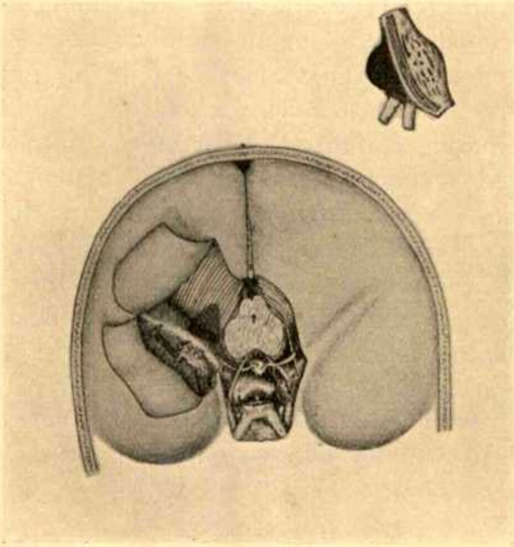

FIG. 4.—Dissection showing the spread of coloured gelatine injected into the Gasserian ganglion post mortem. The spread over the cerebellum and to geniculate ganglion is shown, together with the mass in the Gasserian ganglion.

cases of intracranial lesions of the seventh nerve, as by acoustic nerve tumours, taste was absent. Though the evidence in favour of the seventh nerve carrying taste fibres, evidence which is derived from comparative anatomy, experimental inquiry and clinical observation, seems decisive enough, the loss of taste in so many of these fifth nerve cases is very puzzling, and we feel that no satisfactory explanation has yet been obtained

*Deep pressure pain.*—Deep pressure pain was investigated by means of an algometer. This instrument consists of a rod balanced against a spring graduated to read in pounds; the blunt extremity of the applicator is three-eighths of an inch in diameter (9 5 mm.). In applying this instrument a gradually increasing pressure was exerted at right angles to the area being tested, the patient keeping his eyes closed. The patient was instructed to respond by raising his hand as soon as he felt the pressure becoming painful; the instrument was then removed and read. Pressures over twenty pounds were not attempted owing to the danger of injuring tissues; where no response was made with such a pressure it was recorded as "negative." In the early stages of this investigation the head was supported by a pillow.

Typical readings obtained by this method are illustrated in a case with complete cutaneous loss:

Mrs. C.—Trigeminal neuralgia for several years. Injection of alcohol 1930. Examination two years later. Cutaneous anæsthesia complete. Symmetrical points were tested and gave the following results:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Temporal fossa .. .. .. | 4 lb. | 5 lb. |
| Supra-orbital region .. .. .. | 4 lb. | 10 lb. |
| Above zygoma .. .. .. | 6 lb. | 6 lb. |
| Masseter (non-anæsthetic on both sides) | 5 lb. | 4 lb. |

Many readings similar to this case were obtained, and at first we were inclined to assume that deep pressure pain could still be elicited over the anæsthetic area, and it was natural to infer that the seventh nerve would afford the most likely anatomical pathway for such sensation. Similar investigations and conclusions have been published by others, e.g., Frazier [14], Davis [10], Gerard [16], Maloney and Kennedy [24] *et alia*, and the figures they give are of a similar order to those presented by us.

Our confidence in this interpretation was disturbed when we encountered cases in which the readings were of such an order as to suggest that deep pain was absent when the fifth nerve only was destroyed, and seventh nerve intact, as in the following case:—

Mr. F.—Alcohol injection for trigeminal neuralgia in 1923, and complete anæsthesia of the trigeminal area when investigated in 1932, that is nine years later. An investigation of deep pressure pain with the algometer gave the following readings:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Supra-orbital region | 7 lb. | Negative |
| Infra-orbital region | 8 lb. | 18 lb. |
| Temporal fossa | 9 lb. | 6 lb. |
| Masseter (non-anæsthetic on both sides) | 9·5 lb. | 9·5 lb. |

The discrepancy in the readings from the temporal region led us to reconsider our technique. On re-testing the temporal region with the head firmly supported the readings obtained were:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Temporal fossa | 8 lb. | 11·5 lb. |

This indicated the importance of eliminating the action of the cervical muscles, and thereafter deep pressure was reinvestigated in several of the earlier cases and in all others while the head was voluntarily pushed hard against a rigid resistance. When this was done we found that deep pressure pain could not be elicited over the anæsthetic area. The following cases illustrate this:—

J. R.—Injected with alcohol in September, 1931. Investigated January, 1932. Anæsthesia complete. The following readings were obtained, the head not being held properly rigid:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Temporal fossa | 5 lb. | 8 lb. |
| Supra-orbital region | 4 lb. | 17 lb. |

When the activity of the cervical muscles was excluded by the head being pressed hard against a rigid resistance, the following readings were obtained:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Temporal fossa | 5 lb. | Negative |
| Supra-orbital region | 6 lb. | Negative |
| Infra-orbital region | 7·5 lb. | Negative |

Mrs. C.—Injected March, 1932. Examined one year later. The anæsthesia was complete.

The first set of readings obtained with head improperly supported were:—

| | Normal side | Anæsthetic side |
|---|---|---|
| Temporal fossa | 4 lb. | 5 lb. |
| Supra-orbital region | 4·5 lb. | 10 lb. |

When re-tested with careful control of the cervical muscles the result was:—

| | | |
|---|---|---|
| Temporal fossa | 7 lb. | 17·5 lb. |
| Supra-orbital region | 4 lb. | Negative |

In eight cases results similar to these experiences were obtained and we began to favour the conclusion that the fifth nerve contained the fibres of deep pressure pain the appreciation of which was lost when the ganglion was destroyed. This impression was confirmed by our observations on deep pressure pain over the buccinator. The method adopted was to press the algometer against the outside of the cheek which was supported on the inside by the observer's fingers. By this means we felt justified in believing that the patient could obtain no impression of the amount of pressure exerted through the instrument except from the region to which the instrument was applied. The line of cutaneous anæsthesia crosses the buccinator, and unless care is taken to ascertain that the applicator is in contact with anæsthetic skin the readings may be low, and in crossing the line between the non-anæsthetic and anæsthetic areas over the buccinator there is the greatest difference in the readings. For example, in one case the anæsthetic area over the buccinator gave a reading of over 11 lb., while close by where the skin was non-anæsthetic (falling outside the trigeminal area) the reading was 6 lb.; in another case the same procedure gave 11 lb. over the anæsthetic part and 2 lb. over the adjacent normal area. Thus confirmation was obtained that the fifth nerve subserves the function of deep pain from the face area.

To test this conclusion further the seventh nerve was blocked by injection in five cases. The needle was inserted just in front of the tip of the mastoid process to a depth of about 1·5 cm., and 3 c.c. of 4 per cent. novocain and 1 in 60,000 adrenalin were injected. Complete facial palsy was regarded as adequate evidence of total blocking of the seventh nerve for, as is well known, sensation disappears before the motor loss is observed in such injections. The algometric readings in such cases were in no way altered from readings obtained before the injection of the seventh nerve. An illustrative case is that of E.B.:—

Injected 1932. Complete loss over the maxillary and mandibular areas, partial in the region of the ophthalmic branch. In the anæsthetic region, the algometer readings were:—

| | Normal | Anæsthetic |
|---|---|---|
| Infra-orbital region .. .. .. | 6·5 lb. | Negative |
| Temporal fossa .. .. .. | 4·5 lb. | Negative |
| Supra-orbital region (partial anæsthesia) | 3·5 lb. | 5·5 lb. |

The facial nerve was then injected with 4 per cent. novocaine and 1 in 60,000 adrenalin, with a resulting complete facial palsy, and the following readings were obtained:—

| | Normal | Anæsthetic |
|---|---|---|
| Infra-orbital region .. .. .. | 4·5 lb. | Negative |
| Temporal fossa .. .. .. | 4·5 lb. | Negative |
| Supra-orbital region .. .. .. | 3·5 lb. | 7 lb. |

The addition of a facial block in no way affected the readings over the maxillary and mandibular distributions, and it is interesting to observe that in the distribution of the ophthalmic, where the anæsthesia was only partial, the injection of the seventh nerve gave no significant alteration in the reading for deep pressure pain.

Another series of observations support the suggestion that the fifth nerve carries the impulses recognized as deep pressure pain. In twelve cases of facial palsy due to lesions varying in situation from the stylomastoid foramen to the internal ear, algometric readings on the side of the facial paralysis in no way differed from those obtained on the healthy opposite side.

TABLE OF ALGOMETRIC READINGS IN FACIAL PALSY OF EIGHT YEARS DURATION (FIFTH INTACT).

| | Normal | Palsied side |
|---|---|---|
| Supra-orbital region .. .. .. | 8 lb. | 8·5 lb. |
| Infra-orbital region .. .. .. | 9 lb. | 8 lb. |
| Buccinator .. .. .. .. | 9·5 lb. | 10 lb. |
| Temporal fossa .. .. .. | 8·5 lb. | 7·5 lb. |

From these several observations we conclude that the fifth nerve is the pathway for deep pressure pain from the face area, thus confirming an opinion expressed earlier by Wilfred Harris [17].

*Afferent fibres in the seventh nerve.*—The investigations recounted in the previous section brought us to the conclusion that the impulses of deep pressure pain run in the fifth nerve; this raised accordingly the problem as to the existence of afferent fibres in the seventh nerve, other than those for taste and, if present, what functions they subserved.

The presence of afferent fibres in the seventh nerve has been demonstrated by chromatolytic methods and degeneration experiments (v. Gehuchten [28], Edgeworth [12], Edgeworth and Wakeley [30]). When the fifth is destroyed no ataxia of the ocular muscles has ever been recorded; it can also be shown that no ataxia of facial muscles can be detected. The absence of ataxia of the facial muscles is demonstrable by the fact that our cases with complete destruction of the motor and sensory portions of the fifth nerve were able to carry out alternating movements of the two sides of the face with precision, and could repeat on the anæsthetic side any movement which they had been instructed to carry out on the normal side. Though such patients were unaware of the accumulation of food against the anæsthetic cheek, yet they recognized the displacement if this was brought about quickly by pushing against its inner and anæsthetic surface with a blunt instrument. We were able to demonstrate this satisfactorily in twelve cases; and in four cases the pinching up and stretching rapidly of the anæsthetic skin over the face was immediately appreciated. When the seventh nerve was blocked and a facial palsy induced, these patients were unable to apprehend the distension of the cheek. For these reasons we believe that the afferents in the facial, other than those of the chorda tympani, subserve proprioceptive sensibility, and from our previous observations we further conclude that these fibres do not carry impulses of deep pressure pain.

*Paræsthesia.*—Three cases who had a complete loss of function of the fifth nerve suffered from paræsthesia of a burning and distressing character. In two of these cases the ganglion had been removed at operation eleven and twelve years previously with a resulting complete anæsthesia to all recognized tests over the face, nose and mouth. These two cases do not lend support to the suggestion that the paræsthesiæ only occur in cases with incomplete destruction of the ganglia. Attempts were made to relieve the distressing subjective sensations by blocking the seventh nerve at the stylo-mastoid foramen with novocain, but no alteration in their character or intensity resulted therefrom.

*Blushing.*—It was found that blushing produced by means of suitable stimuli was symmetrical and equal on the two sides of the face in cases with the Gasserian ganglion previously destroyed. The ability to blush equally on both sides of the face was observed in three cases with unilateral cervical sympathectomy; careful observation failed to reveal any difference in time of onset or depth of colour on the two sides in these cases. In patients with a facial palsy, two exhibited no difference in blushing on the two sides, two had a greater depth of colour on the healthy side, and one case previous to the test had a general flush noticeable on the palsied side.

Blushing therefore appears to be independent of the integrity of the fifth nerve and sympathetic. Observations in cases of facial palsy are as yet too few to warrant any conclusion, and this work is being carried further by a series of pharmacological and thermometrical experiments.

*Accessory pathways of pain.*—Recent medical literature contains frequent references to the possibility of other pathways for pain than the trigeminal nerve from the region of the face. Davis [10] in experimental work on cats suggested that the seventh nerve may subserve pain and offered clinical evidence in favour of his conclusions. It is possible that the responses of the cats in his experiments, in which the face area was stimulated with buried electrodes after cutting the fifth nerve, may have been due to proprioceptive sensation and not necessarily to pain. Our investigations, as recorded in previous paragraphs, do not lend support to the suggestion that the seventh nerve carries impulses of pain from the face. More recently the sympathetic system has been suggested as a pathway by which pain may reach the central nervous system. The evidence offered by Foerster, Altenburger and Kroll [13] is not convincing. Frazier and Helson [15] observed the presence of the appreciation of painful hot stimuli in cases where there was anæsthesia over the maxillary and mandibular distribution, but its absence when the superior cervical ganglion had been removed as well. Since in these cases there had been only a partial resection of the central root, the observations do not prove that the inability to appreciate the hot stimuli was due to the sympathectomy.

In five cases in which the cervical sympathetic had been severed by operation for the removal of the stellate ganglion or by accidental severance of the cervical sympathetic trunk, we have been unable to obtain any difference in testing the two sides of the face by means of graded stimuli for superficial pain and deep pressure pain. Such observations are in accord with the experimental work of Davis and Pollock [9], and the conclusions of Langley [23], and the investigations of Ranson and Billingsley [26] and Cleveland [6]. These few observations, along with the experimental work quoted above, confirm our belief in Langley's contention that the cervical sympathetic is an efferent mechanism only.

The oculo-motor nerves are also a possible route by which painful sensations from the orbital region may reach the brain. That they contain afferent fibres has been demonstrated in animals by Sherrington and Tozer [27] and Woollard [31]. Following a complete destruction of the Gasserian ganglion in man, Davies [8] records a case in which the eye on the anæsthetic side was extirpated without further anæsthetization; we had a similar case. Again, pressure over the eyeball on the anæsthetic side fails to arouse pain. Diplopia never resulted from destruction of the fifth nerve in our cases; accurate fusion of the visual images may be regarded as an extremely delicate test of co-ordination of the eye musculature. On these facts one may state that the afferents in the oculo-motor nerves do not subserve pain but are probably concerned with afferent impulses requisite for accurate co-ordination of eye movements—in other words, the oculo-motor nerves do not serve as an accessory pathway for pain.

Our observations fail to demonstrate the presence of a pain pathway in the oculo-motor nerve, the facial nerve, and the sympathetic. The trigeminal nerve thus remains the nerve for all painful impulses from the face region.

## SUMMARY.

(1) The fifth nerve is the general cutaneous nerve of the head region; the ophthalmic, formerly a separate nerve, is the most rostral of the body.

(2) In ten cases of injection of the Gasserian ganglion there was complete destruction of the ganglion as judged by the extent and completeness of the anæsthesia. The longest duration of the anæsthesia was ten years.

(3) Evidence is produced to strengthen the idea that all reflexes dependent on the ophthalmic division require a stimulus which in normal subjects is felt as pain.

(4) The problem why a number of patients after destruction of the Gasserian ganglion lose taste on the anterior two-thirds of the same side of the tongue is discussed.

(5) Evidence is presented to show that deep pressure pain depends on the integrity of the fifth nerve only.

(6) The conclusion is drawn that the afferent fibres in the seventh, other than taste, and in the third nerve, subserve a proprioceptive function and do not convey pain impulses.

(7) Blocking of the seventh nerve has no influence on the paræsthesia following destruction of the Gasserian ganglion.

(8) Throughout the investigations no evidence was obtained that impulses subserving pain in the face and orbit follow any pathway other than in the fifth nerve.

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# THE LOCALIZATION OF THE PATHS SUBSERVING MICTURITION IN THE SPINAL CORD OF THE CAT.

BY F. J. F. BARRINGTON.

*(From the laboratories of the Surgical Unit, University College Hospital Medical School.)*

## I.—HISTORY.

BUDGE (1864) stated that, after removal of the dorsal half of the cord at the level of the fifth cervical vertebra in a newly born bitch, stimulation of the remaining ventral half evoked movement of the bladder, rectum and tubes. He describes one experiment only.

Mosso and Pellacani (1882) showed that division of rather more than the ventral half of the cord in the posterior thoracic or anterior lumbar region of the dog did not abolish the contraction of the bladder evoked by pressure on the fore limbs, whereas division of the dorsal half did; they concluded that the motor fibres for the bladder pass by the dorsal columns or by the dorsal part of the lateral columns.

Stewart (1899) made experiments on cats. He found that when the pelvic nerve and the lumbar splanchnic nerves on the same side were divided and a hemisection of the cord made in the posterior thoracic region, stimulation of the cord in front of the hemisection produced contraction of the bladder whether the hemisection had been made on the same side as the divided nerves or on the opposite side. He concluded that there must be a partial crossing of the efferent fibres behind the level of the hemisection. In order to determine the most posterior limit of this crossing, he divided the nerves on one side, made a hemisection on the other and stimulated the cord in front of the hemisection: he then divided the cord in the median sagittal plane backwards from the hemisection, in stages, until stimulation ceased to produce a bladder contraction though stimulation behind the hemisection on the same side still remained effective. The level determined in this way was that of the most posterior strands of the fifth lumbar root. By splitting the cord in the same way but from behind forwards the anterior limit of the crossing was found to be just behind the origin of the second lumbar root. The limits of the crossing were the same for impulses passing by the sympathetic as for those passing by the sacral nerves.

By making a hemisection at the first cervical root and another on the opposite side at the twelfth thoracic and stimulating in front of the first, he showed that there was no crossing between these two levels. He found that stimulation of the cord in front of a complete hemisection on one side and a cut involving all the cord except the dorsal column on the other, anterior to the level of the second lumbar root, was ineffective in producing a bladder contraction. Stimulation in front of a hemisection on one side and a cut involving the ventral half of the cord on the other, was effective in giving rise to a bladder contraction as it was also when the middle third (dorsal and ventral columns) of the remaining side had been divided instead of its ventral half. On dissecting the dorsal half of the lateral column free from the rest of the cord and stimulating it, contractions of the bladder occurred. Division of the lateral column at the fifth and sixth lumbar roots abolished the contraction of the bladder produced by stimulating the cord in the dorsal region after the lumbar nerves to the bladder had been cut, but division of the middle third of the cord did not. Stewart therefore concluded that impulses pass down the cord to the bladder in the dorsal part of the lateral columns.

Spiegel and Macpherson (1925) experimented on decerebrate cats. They produced contractions of the bladder by stimulation of the cerebral peduncles and noticed the effect on this of lesions in the anterior thoracic region of the cord. Destruction of the dorsal and ventral columns and of the grey matter and of Lissauer's zone did not abolish the contractions, but destruction of the lateral columns did. A hemisection in the cervical region with one on the opposite side in the posterior thoracic region abolished contraction.

## II.—METHODS.

In all the experiments referred to in the previous section it is only the centrifugal path which is demonstrated. Impulses, produced artificially, passing from the cord to the bladder are shown equally whether they in fact occur in micturition or whether they do not: for instance, Stewart demonstrated impulses passing to the bladder by the sympathetic, but as it is known that the sympathetic supply to the bladder can be cut without producing any defect in micturition, it is open to question if such impulses take place during micturition. In none of the experiments were the animals kept a sufficient time for the partly damaged parts of the cord to recover; there must therefore have been a loss of function during the experiments of a greater part of the cord than that actually found destroyed at the post-mortem examination.

To obviate these objections lesions were made in the cord, the cat kept alive, and the presence or absence of any defect of micturition noticed. Female cats were used in most cases. A defect might therefore be due to the destruction of the centrifugal or of the centripetal path, or of both. Two principal defects were found, the presence of residual urine and loss of consciousness of the need to micturate: residual urine, in some experiments, occurred by itself, but loss of consciousness of the need to micturate was never observed as a result of a lesion of the spinal cord in the absence of residual urine. The existence of residual urine was determined by feeling the bladder a short time after the cat had been known to have passed urine. In this way the volume of residual urine can be roughly estimated; when it was necessary to estimate the residual urine with accuracy the bladder was emptied by expression over a vessel. An intact cat at liberty in a room, on the floor of which is one of the trays of sawdust on which the cages habitually stand, will always micturate on this tray; cats who passed urine indiscriminately on different parts of the floor were assumed to have lost the consciousness of a desire to micturate.

This method is open to the objection that a part of one or both paths may be destroyed without producing an objective defect in micturition, and conversely that what appears to be a complete abolition of micturation may result when some part of the specific region of the cord is still intact. This objection can be overcome by making several experiments in the same level of the cord.

For making the lesion, the cat was anæsthetized with chloroform and the anæsthetic then changed to ether. The appropriate vertebral lamina was removed and the dura opened. The lesion was generally made either with an electro-cautery needle, or with a needle which was made the cathode of an electrolytic circuit, an indifferent anode being placed on a hind limb; these methods were found better than mechanical ways of making the lesion. The extent of the lesion was determined after killing the cat with chloroform, tying a cannula into the aorta and washing the vessels through first with warm, normal salt solution and then with 10 per cent. formalin. The part of the cord concerned was removed, embedded in paraffin, sections $10\mu$ thick cut and mounted at each quarter of a millimetre and stained with Ehrlich's hæmatoxylin and eosin.

Lesions of the cord made in this way often, if not always, temporarily abolish the function of some part of the spinal cord not actually destroyed, presumably by interference with its circulation. When an experiment is made for the purpose of determining localization it therefore becomes a matter of first importance to know how long a defect in function produced in this way can last, otherwise such a defect may be wrongly attributed to the absence of function of the destroyed part of the cord. The following accounts are those of two of the three experiments in which the period of recovery from a defect in micturition following operation on the spinal cord were the longest observed. The third experiment is described at the end of Section 5, and its period of recovery was intermediate between the two following:—

*Experiment* 1.—A lesion was made in the third lumbar segment with an electro-cautery needle, the dura having been opened on the left side. At the post-mortem examination the destroyed part of the cord on the left side was found to be the grey matter, except the tip of the ventral horn, the lateral column except a small part of it adjacent to the ventral column, and the dorsal column, except a small part adjacent to the central grey matter. The central grey matter was destroyed on both sides, but otherwise there was no destruction of the right side of the cord.

On the sixth day after the operation, there having been no voluntary movements of either hind limb, the cat had become soaked with urine. Chloroform was given, 160 c.c. of urine was obtained by expressing the bladder and rather less than that quantity left in.

On the eighth day he was again soaked with urine. Seventy c.c. of urine were expressed from the bladder and about the same volume left in. On scratching the back of one pinna there was no movement of the homolateral hind limb on either side.

On the thirteenth day he was soaked with urine. The urethral resistance was felt to be marked on attempting to express the bladder. Chloroform was given and the bladder nearly emptied by expression, 145 c.c. of urine being obtained. On scratching the back of the right pinna there was flexion of the right hip.

On the fifteenth day the cat was again wet and he dripped urine when picked up. Chloroform was given, the bladder nearly emptied by expression and 85 c.c. obtained.

On the nineteenth day he was wet. Expression of the bladder was begun. After the stream had started it continued spontaneously after removal of the pressure, but some residual urine was left, this was subsequently expressed. He could make walking movements with the right hind limb in progression if the pelvis was raised by holding the tail up.

On the twentieth day the bladder was found to contain about 20 c.c. and to be very hard; urine escaped directly it was compressed.

On the twenty-sixth day he could walk on three legs dragging the left hind limb after him. When 15 c.c. of urine had been passed within the previous 1¼ hours the bladder felt to contain 30 c.c.; feeling it led to the escape of urine in a continuous stream which continued after the pressure was removed. The stream stopped before the bladder was empty and about 15 c.c. were left in, which were expressed.

On the thirtieth day he made walking movements with the left hind limb.

On the thirty-first day he passed urine at least three times, from 10 to 25 c.c. being passed each time. When 15 c.c. had been passed within the previous half-hour the bladder was completely emptied by expression and 10 c.c. of residual urine obtained.

On the forty-ninth day he probably only passed urine twice and certainly passed 35 c.c. at one micturition.

On the fifty-seventh day, when he was loose in the room, he was seen to pass urine on a tray of sawdust, provided for the purpose, on two occasions, the bladder not being palpable after. This was seen again with the same result next day.

On the sixtieth day he showed stiffness in movement of the left hind leg in walking which, when he hurried, at times adducted and let his pelvis down on the left side.

The residual urine, therefore, persisted until the thirty-first day, and had disappeared by the fifty-seventh. The cat passed from the stage of retention with overflow to normal micturition through a stage of frequency of micturition with a diminishing volume of residual urine. The frequency was greater than could be accounted for by the residual urine.

*Experiment* 2 (fig. 6).—A lesion was made in the first lumbar segment with an electrocautery needle, the dura having been opened on either side. At the post-mortem examination the destroyed part of the cord on the right side was found to be periphery of the dorsal part of the lateral column for rather more than half its extent except for a thin strip touching the dorsal root; the lateral column was destroyed for rather more than half its thickness at the dorsal side, but the lesion tapered to a point ventrally. On the left side the destroyed part occupied the periphery of the lateral column for about its dorsal fourth; the maximum thickness of the destroyed part was rather less than a quarter of the lateral column.

On the first day after the operation the cat could walk, but frequently put the dorsa of the right hind toes on the ground.

On the third day urine was passed for the first time; within two hours of passing 5 c.c. the bladder felt as if it contained 100 c.c.

On the forty-ninth day within half an hour of passing 30 c.c. the bladder felt as if it contained 20 c.c.

On the sixtieth day she was seen to pass 55 c.c. Chloroform was given immediately after and the bladder emptied by expression of 25 c.c.

On the sixty-fourth day, 75 c.c. having been passed within the previous quarter of an hour, the bladder could not be felt. This was the first occasion on which this had occurred since the operation.

On the seventy-first day, 40 c.c. having been passed within the previous half hour, the bladder felt as if it contained 25 c.c.

On the eightieth day, 55 c.c. having been passed within the previous fifteen minutes, the bladder felt as if it contained 20 c.c.

On the hundredth day, immediately after passing 75 c.c., the bladder could not be felt.

Subsequently observations were made on numerous occasions and no residual urine detected. When at liberty she passed urine on a tray of sawdust. She was killed on the 157th day.

In this experiment, therefore, there was retention of urine with overflow. A small volume of residual urine was subsequently present, constantly up to the sixty-fourth day and intermittently up to the eightieth; after the hundredth it was constantly absent.

It is, therefore, improbable that a transitory defect in micturition due to a lesion of the cord will last more than eight weeks, but it certainly may last more than eleven and possibly even fourteen weeks. It follows that when a defect occurs conclusions with regard to localization cannot be drawn from experiments done for observations on degeneration by the Marchi method, since in this case the cat must be killed within three weeks.

## III.—The Level of the Anterior End of the Deep Origin of the Efferent Fibres of the Pelvic Nerve.

Elliott (1907) made spinal transections in the posterior lumbar and anterior sacral regions and later examined the pelvic nerves for degenerated fibres. As a result of four experiments he concluded that no motor cells of the pelvic nerve are situated in front of the spinal root origin of the great sciatic nerve.

Before repeating these experiments seven experiments were made to find the most favourable period after the lesion for finding degenerated fibres. The sacral spinal roots were divided or excised on one or both sides and the cats killed after a variable number of days. The pelvic nerves were put into 1 per cent. osmic acid directly after death and left there from twelve to twenty-four hours. After prolonged washing a small piece was put into 40 per cent. methyl alcohol and left there for two or more days. It was teased in 40 per cent. methyl alcohol, treated with 80 per cent. ethyl alcohol followed by ascending strengths up to absolute and mounted in Gurr's medium. One cat was killed in three days, one in five days, and the remaining five in eight to thirteen days. In three days there was no visible change, in five days there was well-marked breaking up of the myelin into globules, but these stained little if at all darker than normal myelin; in the remaining five cats the changes were greater the longer the period. It appeared, however, that eight days was the best period for the purpose, since the black fat droplets were so far apart after longer periods that if only a few degenerated fibres were present, it might be possible to overlook the fact that they were nerve fibres.

Seven transections were made, the cats killed in eight days and the nerves examined for degenerated fibres. The results are shown in the table :—

TABLE.

| Spinal segments involved in the transection | Sacral roots from which the pelvic nerves were found to arise by dissection | Degenerated fibres |
|---|---|---|
| 4th and 5th lumbar .. .. .. | 1 and 2 | Absent |
| Posterior part of 5th lumbar .. .. | 1 and 2 | Absent |
| 6th lumbar .. .. .. .. | 2 and 3 | Absent |
| 6th lumbar .. .. .. .. | 2 and 3 | Numerous |
| 6th lumbar .. .. .. .. | 1 and 2 | Few |
| 6th lumbar .. .. .. .. | 1 and 2 | Numerous |
| 1st sacral .. .. .. .. | 1 and 2 | Numerous |

The pelvic nerve in the cat commonly arises from all three sacral roots (Sherrington, 1892) (Langley and Anderson, 1895). In the experiments just described the cats were dissected after the vessels had been washed through with formalin. It seems probable that the third root, which is very fine, was ruptured in consequence of the fragility produced by the formalin and so overlooked. It appears safe, however, to infer that the two roots given were the two larger.

No conclusions can be drawn from experiments in which degenerated fibres were present, since softening extends forward and backwards from the plane of the transection for a variable and unknown distance. Softening backwards from the transection was noted as being extensive in the fourth and in the sixth experiment. It follows from these experiments that there may be two, but there cannot be three, complete spinal segments intervening between the segment from which the more anterior of the two larger roots of the pelvic nerve arises and that which contains the most anterior part of the deep origin of its efferent fibres.

A lesion better defined than a transection can be made by inserting a needle through the dorsal columns and making it the cathode of an electrolytic circuit. Four experiments were made in this way, the cats killed in eight to ten days and the destruction of the grey matter confirmed and the limit of the lesion determined by microscopical examination. In the first and second the lesion was in the 6th lumbar segment; the pelvic nerves arose from the second and third sacral roots in one and the first and second in the other and no degenerated fibres were found in them. In the third the lesion was in the last lumbar and first sacral segments; the pelvic nerves arose by a large branch from the second sacral, one nearly as large from the third and a very fine branch from the first sacral; one pelvic nerve contained one degenerated fibre and the other none, the single degenerated fibre was one of the thickest that occur in the nerve and therefore probably afferent. In the fourth the lesion was in the seventh lumbar and first sacral segments, the pelvic nerves arose from the second and first sacral segments, six degenerated fibres were found on one side and two on the other; the teasing was not very efficient in this experiment and it is possible more degenerated fibres were present, but not more than twice the number stated. It appears, therefore, that no efferent fibres of the pelvic nerve arise as far forward as one clear segment in front of the more anterior segment from which the two larger roots of the pelvic nerve arise. In none of the three experiments mentioned was there any diminution in the urethral resistance as far as could be felt from squeezing the bladder, showing that at least the chief part of the nucleus of the dorsal nerve must have been behind the lesion in all experiments.

## IV.—The Anterior Lumbar Region.

For the purpose of this paper the anterior lumbar region of the cord means the last, or thirteenth, thoracic, and the first two lumbar segments. It is the part of the cord from which the first three pairs of roots immediately behind the ribs arise, and, in most cats, the part immediately in front of the origin of the most anterior of the efferent fibres to the bladder, though in a certain proportion the second lumbar root gives a branch to the sympathetic supply of the bladder (Sherrington, 1892) (Langley and Anderson, 1895).

The extent of the part of the cord destroyed at this level in each of fifteen cats is shown as a dotted area in figs. 1 to 15. The segment involved, and in cases where a permanent defect in micturition followed the operation, the number of weeks after the operation for which observations were made are also shown. In the case of Nos. 1 to 4 the cats had both residual urine and loss of consciousness of the need to micturate as long as observations were made. In Nos. 5 to 9 neither of these defects were present when the cat was killed. In Nos. 10 to 15 residual urine was present as long as observations were made, but there was no permanent loss of consciousness of the need to micturate.

If a lesion such as those in Nos. 1 to 4 is unilateral the cat carries the tip of the tail deflected towards the side of the lesion. When the movements of the homolateral hind limb are affected the most frequent condition is that the dorsa of the toes are dragged on the ground in bringing forward the limb for walking; if the affection is greater the dorsa of the toes are stood on when the body is moving forwards on this limb. The affected limb may remain stiff and rather slow in its movements. When the lesion is bilateral the tail is often arched over the back instead of pointed straight up when the cat is pleased; in No. 1 this was so marked that the tip touched the back in the region of the scapulæ.

The effect on micturition of bilateral lesions of the position and extent as those in Nos. 1 to 4 is that retention of urine occurs and progresses to overflow. Hæmaturia, sufficient for the blood to be visible to the naked eye, is not uncommon at this stage. The cat is continually soaked with urine and shows no sign of pain even if the bladder is squeezed. After a period, which may be only three days and is never more than two weeks, urine is passed in jets at intervals. The appearance at this stage is associated with a diminution in the volume of residual urine and in the urethral resistance which can be felt if the bladder is squeezed. The volume of urine passed at micturition in normal cats has great individual variations. In seven experiments the volumes of urine passed at micturition were observed before the operation: the volume of residual urine after the operation and after the passage of urine in jets had become established was about the same as that passed at micturition in two of these and less in five. If, as in Nos. 1 to 4, the lesions are not extensive enough to seriously affect the cat's movements, jets of urine are usually passed while the cat is walking about. Each time a jet passes there is a momentary pause in walking with a slight lowering of the pelvis or movement of the base of the tail, or both together. The cat appears quite unconscious of passing urine and makes no attempt to bury it unless it accidentally comes across the puddle in the course of its further wanderings. Pleasure and anger both seem to lead to the passage of jets of urine. Jets can be evoked by scratching the cat's head or stroking its back, and they occur when it is evincing pleasure for no apparent reason either by rubbing its sides against vertically situated objects or by kneading with its fore paws; they also occur if the cat has seized a piece of meat and is growling at the approach of another cat. The passage of a jet is not immediately produced by a straining movement such as jumping. The cats never select places on which to pass urine. Though the amount passed in each jet is small, probably more often 2 c.c. than 5 c.c., a considerable volume of urine may be passed in a short period because numbers of jets occur at short intervals. Urine is either not at all, or only rarely, passed during sleep. For these reasons a considerable volume of urine is usually passed within a short period after work has started in the animal house in the morning. Cats with such lesions may be soiled with urine and fæces round the perineal region, but this is not usually the case. If cystitis supervenes from a naturally occurring infection the residual urine diminishes almost to nothing and the perineal region becomes soiled with urine owing to its passage becoming nearly continuous.

No. 4 was conscious of needing to defecate, but its sensations in this respect were imperfect, for though he would squat on the sawdust tray defecation would not take place until after he had got up and was going away. No notes were made on defecation in Nos. 1, 2 and 3, but in another cat, whose lesions are not figured, there was certainly no consciousness of wanting to defecate since she would do this anywhere: the smaller of the two lesions in this cat was in the position of those in No. 4, but extended slightly deeper into the cord.

In three cats with such lesions, including Nos. 1 and 3, and in two others having the inferior mesenteric ganglia excised in addition, a spinal transection was made in front of the lesion in the ninth, tenth or eleventh thoracic segment. In one of these one observation only was made on the twelfth day after the transection and the residual urine was found to have increased from 65 to 80 c.c. before the transection to 200 c.c. after. The remaining four were each observed on three to eight occasions after the transection. On one occasion in each the volume of the residual urine showed a marked increase over that present before the transection, but on all the other occasions it was approximately the same after as before the transection. It therefore appears that after the transection the volume of the residual urine may, on occasions, be considerably greater than before it, but that at most times it is about the same. It seems probable that the occasional increase arises from the diminished activity of the cat resulting from the transection producing a diminution in the frequency with which the passage of jets of urine is reflexly evoked. In four of the five cats it was noted that in the early days after the transection the urethral resistance, felt on squeezing the bladder, was low, as it had been before the transection : had the transection been made in a previously intact cat the urethral resistance at this stage would have been high. The fifth cat was exceptional in that the palpable urethral resistance was considerable both before and after the transection.

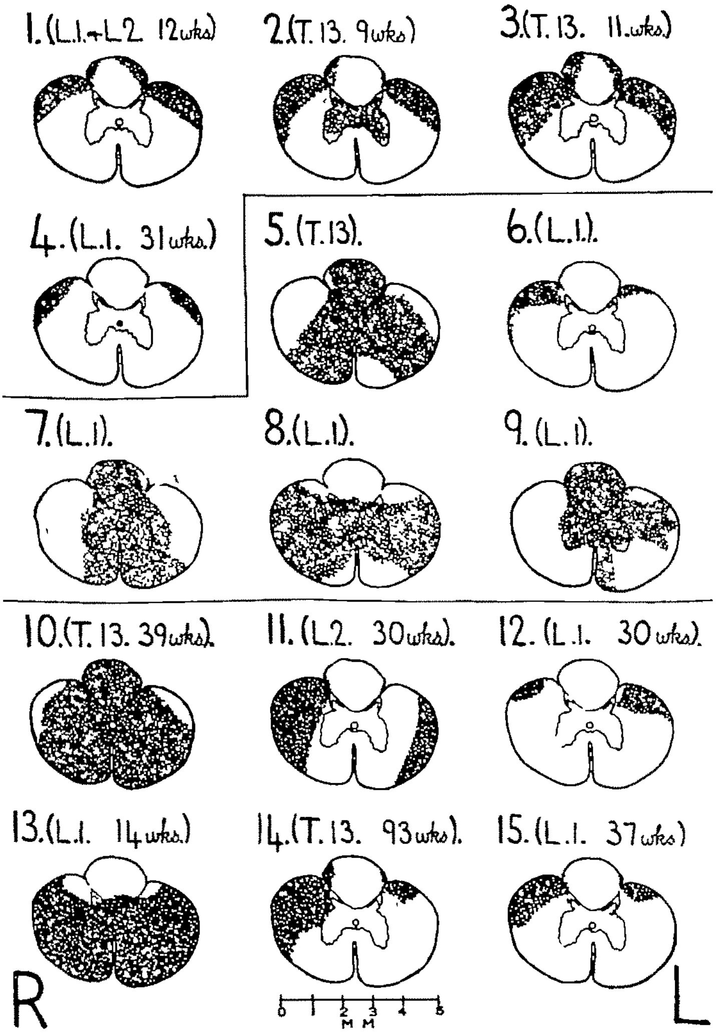
If the inferior mesenteric ganglia are excised at the same time as a lesion such as those in Ncs. 1 to 4 is made no obvious difference in the course of events described occurs. The inferior mesenteric ganglia were excised in three cats in which the lesions had been made from fifty to one hundred and eight days previously, one being No. 2 sixty days after the lesions had been made; in one a slight, and in two a marked, diminution in the residual urine followed.

If the pudic nerves are divided after a lesion, as those in Nos. 1 to 4, has been made and the urine has come to be passed in jets, the passage of urine in jets ceases and the urine runs away in drops which are faster during straining movements; if previously clean, the perineal region becomes dirty and movements associated with passing jets, such as lowering of the pelvis and depression of the base of the tail, do not occur.

In one cat lesions were made in the position described and the inferior mesenteric ganglia excised; in ninety-five days the pelvic nerves were divided. This was followed by a great increase in the residual urine and in the urethral resistance, felt on squeezing the bladder. In four other experiments the pelvic nerves, dorsal sacral spinal roots or one on one side and the other on the remaining, were divided at the time of making the lesions or before. The urethral resistance remained high for ten to thirty-three days, and when it did diminish cystitis was present.

The effect of division of each of the three pairs of nerves on the condition resulting from these lesions is therefore exactly the same as the effect on the condition which follows a complete transection (Barrington, 1931). It may therefore be concluded that all the effects on micturition which follow a complete transection of the cord are due to the destruction of a small part of it and that this part has been largely or completely destroyed in each of the cats Nos. 1 to 4. This conclusion is supported by the fact that the condition resulting from the lesions, as far as micturition is concerned, does not differ from that resulting from a spinal transection.

When the positions of the lesions in Nos. 1 to 15 are used for the purpose of localizing the micturition paths it must be remembered that since a unilateral lesion, however extensive, causes no defect in micturition the whole or a large fraction of the paths must have been destroyed on both sides in experiments in which a permanent defect in



micturition results, whereas the paths may have been spared on only one side in experiments in which no such permanent defect results.

The only part of the cord destroyed on both sides in each of Nos. 1 to 4 is that destroyed on the left side of No. 4, namely, a part of the dorsal half of the lateral column extending from the periphery inwards for one-fourth or less of the thickness of the column, nearly reaching the dorsal root dorsally and to the middle of the periphery of the column ventrally. The whole or a large part of either the centrifugal or centripetal path or of both must therefore be in this part of the cord. Nos. 5 to 9 show that no large part of either path can be in any region of the cord except in the dorsal half of the lateral column, since in one or other of them all other parts are destroyed on both sides. The only point in localization left to consider is whether either path is situated in any other part of the dorsal half of the lateral column than that just described.

In No. 10 the destroyed and undestroyed parts are nearly the reverse of those in No. 4. If, therefore, the whole of both paths are in the part of the cord destroyed in No. 4, No. 10 should have had no permanent defect in micturition.

No. 10 was a castrated male. Retention of urine followed the operation and overflow occurred on the third day after the operation. He was then given chloroform and the bladder emptied by expression to 220 c.c. of residual urine. Overflow recurred on the fifth day, when expression of the bladder under chloroform gave 90 c.c. of residual urine. On the sixth day, within an hour and a quarter of passing 20 c.c., the bladder felt as if it contained 10 c.c. Up to the thirteenth day he continued passing small volumes at a time, and whenever the bladder was felt he seemed to have a volume of residual urine varying from 10 to 40 c.c. By the twentieth day he was passing larger volumes of urine at a time, and on that day, for the first time, no residual urine could be felt after he had passed 45 c.c. From then onwards until the last observation, on the two hundred and sixty-sixth day, residual urine was sometimes absent, but more often present, though the volume was usually only about 10 to 15 c.c.; the volume of urine passed at each micturition increased slightly after the twentieth day. Following the operation, the hind limbs were kept flexed at the hips and fully extended at the knees and ankles, they were rigid and not used in progression. On the nineteenth day it was found that, if his pelvis was supported by holding up the tail, he made appropriate movements with the hind limbs on walking, better with the right limb than with the left. On the sixty-third day he could stand on all four limbs, but could not walk with the hind ones. On the seventy-eighth day he was brought down to the working room, where he remained until the hundred and eighteenth. During this period he passed urine and fæces wherever he happened to be sitting or lying, and never made any attempt to get to the sawdust tray or any other special place. He never, however, made any attempt to move his position except when he heard the attendant bringing his food; if he were then in his cage with the lid open, he would climb out actively, using the fore-limbs only; the side of the cage was 36 cm. high. He licked himself all over, including the paralysed hind limbs. On the two hundred and twenty-third day he could get up on all four limbs, but when he started to move the hind limbs let the pelvis down, because they moved too slowly to correspond with the movements of the fore limbs. He was again brought down to the working room on the two hundred and thirty-ninth day and kept there until he was killed. He was seen to pass urine in the squatting position as other cats do. When he passed urine or fæces outside his cage, he did it on the sawdust tray. It seems that the persistent presence of a small volume of residual urine intermittently must be attributed to destruction of part of a micturition path, and not to an indirect effect arising from the affection of his skeletal muscles, since micturition did not appear affected by this, and since such a defect did occur in other experiments when there was no impairment of locomotion.

As the comparisons of Nos. 10 and 4 leave some doubt about the extent of the paths, the extent of the centrifugal path in the anterior lumbar region was investigated by the old method of observing what lesions in this region abolished the contraction produced by stimulation of the cord in front of it. In four cats lesions were made in the anterior lumbar region sixteen to twenty weeks before the final experiment. All four had persistent residual urine and persistent loss of consciousness of the need to micturate. The hypogastric nerves were divided and the cord transected in the eighth to eleventh thoracic segment under chloroform: decerebration was performed and the chloroform stopped. A wide opening was made in the left side of the abdomen and the bladder observed directly. In two cases contraction occurred with stimulation and in two it did not.

The extent of the smaller lesion in the first two were respectively:—

(1) The periphery of the dorsal half of the lateral column not quite reaching the dorsal root and extending into the column for rather more than a quarter of its thickness, and

(2) The periphery of the dorsal half of the lateral column reaching the dorsal root and extending inwards for less than a quarter of its thickness.

The extent of the smaller lesions in the second two were respectively:—

(1) The dorsal half of the periphery of the lateral column not quite reaching the dorsal root and extending inwards for about a third of its thickness.

(2) The dorsal half of the periphery of the lateral column reaching the dorsal root and extending inwards for about a third of its thickness.

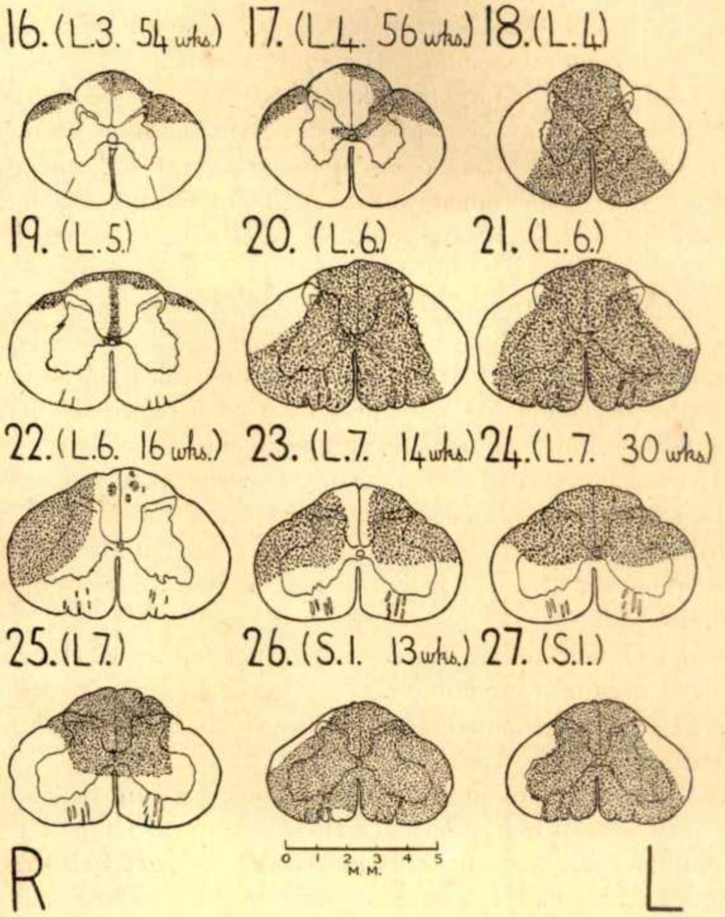
The position and extent of the centrifugal path in the anterior lumbar region is therefore the periphery of the dorsal part of the lateral column, except a small part touching the dorsal root, and it extends inwards for about a third of its thickness. The deep part of this region was not destroyed in No. 4 and was destroyed in No. 10. No. 10 shows that no considerable part of the centripetal path can exist in any other part of the cord since the micturition defect it exhibited was so slight.

Nos. 5 to 9 had no permanent defect in micturition, and of these Nos. 5, 7 and 9 had no defect at all. No. 6 has been fully described in Section 2, and No. 8 had residual urine up to the 18th to the 27th day. Hence the only two of the five that had residual urine which disappeared were the only two that had part of the periphery of the dorsal half of the lateral column destroyed on both sides.

No. 10 has already been described. No. 11 had retention with overflow followed by the presence of residual urine which disappeared as far as could be felt on the thirty-sixth day. When killed, half an hour after micturition, 15 c.c. of urine were present in the bladder although this had not been felt before. He was very fat, so it is possible that a small volume of residual urine was repeatedly overlooked. He was conscious of wanting to micturate but not of micturating, since he would pass urine on the sawdust tray sometimes while standing on it before he had begun to scratch the sawdust, sometimes while still standing and actually scratching the sawdust and sometimes when standing just after he had squatted but passed no urine. His consciousness of a need to defecate was more defective still since fæces was usually passed in an unselected place and not on the tray. The remaining four cats had greater defects in micturition corresponding to the greater part of the periphery of the dorsal half of the lateral column destroyed on either side. They all had retention with overflow followed by the persistence of residual urine, which was very small in amount in No. 15, and they all either retained or recovered the consciousness of needing to micturate. No. 13 was probably unconscious of needing to defecate, and No. 14 was certainly conscious of it. The experiments in which incomplete defects in micturition occurred therefore confirm the supposition that both the centrifugal and the centripetal paths are situated in the part of the dorsal half of the lateral column extending inwards for a third of its thickness. The dorsal portion of this part of the cord is peripheral to the crossed pyramidal tract.

### V.—The Posterior Lumbar Region.

Figures 16 to 27 show the position of lesions behind the second lumbar segment in each of twelve cats. Lesions in the sacral region, particularly posteriorly, which are followed by micturition defects are of little use in localization since there is no adequate method of controlling the integrity of the sacral spinal roots after the lapse of months and the



probability of their injury affecting micturition increases from before backwards.

No. 16 was a castrated male. A large volume of residual urine persisted, and as long as he lived he was unconscious of needing to micturate and of micturating. He commonly passed urine in jets, but besides this, at times, considerable volumes would be passed in a long stream. Sometimes through the abdominal wall the bladder could be felt to harden and a further considerable volume of urine was then passed. The last two facts seem to show that the destruction of the micturition paths was incomplete, and this corresponds with the destroyed part of the cord involving less than the dorsal half of the periphery of the lateral column. His anus was patulous and often fæces could be seen within it for hours before any were passed. He sometimes passed, or endeavoured to pass, fæces in selected places. This, together with the fact that he resented having pressure made on his colon through the abdominal wall though not on his bladder, shows that he preserved at least some sensation of needing to defæcate.

No. 17 had a large volume of residual urine and was unconscious of micturating and of wanting to micturate. She was clean and did not become soiled with urine or fæces. The segment involved was the third lumbar and not the fourth; it has been recorded as the fourth, as fourteen thoracic segments were present instead of thirteen, together with the usual number of eight cervical segments.

No. 18 had no residual urine. No steps were taken to find whether or not he was conscious of needing to micturate.

No. 19 had residual urine for three weeks but not after four weeks. No steps were taken to see whether or not she was conscious of wanting to micturate.

No. 20 had no residual urine. It was not known whether she was conscious of needing to micturate.

No. 21 had no residual urine and was conscious of needing to micturate.

No. 22 also had a lesion in the last thoracic segment which involved the dorsal two-thirds of the left lateral column for about half its thickness from the periphery inwards and which did not quite reach the dorsal root. She had retention of urine with overflow followed by residual urine and was unconscious of wanting to micturate.

No. 23 had residual urine and was unconscious of the need to micturate.

No. 24 had residual urine, but knew both when she wanted to micturate and when she was micturating.

No. 25 had retention of urine with overflow: residual urine followed but its volume was very small after the first two weeks and it was absent in seven weeks. She retained, or more probably recovered, consciousness of the need to micturate. She occasionally lost a few drops of urine while walking about.

In No. 26 the anterior end of the lesion was in the seventh lumbar segment and the destruction of the grey matter extended antero-posteriorly for about six millimetres, so it is unlikely that it extended into the second sacral segment. The pelvic nerves were found by dissection to arise by a large branch from the second and a small one each from the first and the third sacral roots. Retention with overflow occurred and the compressor urethræ was not paralysed, as could be felt by squeezing the bladder. Residual urine persisted. Ultimately she generally passed urine on the sawdust tray, but she sometimes used to walk about before she had finished micturating. She therefore was conscious of the need to micturate but not of micturating. At times she used to lose a little urine while sitting down.

No. 27 had no residual urine. The pelvic nerves were found by dissection to arise by a branch from the first and another from the second sacral nerves, that from the second being the larger.

The results of these twelve experiments are therefore consistent with the paths of micturition being in the same position as in the anterior lumbar region. Nos. 26 and 27 cannot be compared, since although No. 27 appears to have had the more anterior lumbo-sacral plexus the posterior limits of the lesions in the two cases were not recorded sufficiently precisely for comparison. It may be concluded that both centrifugal and centripetal paths are in the periphery of the dorsal half of the lateral columns in the third, fourth and fifth lumbar segments, that they must be within the dorsal three-quarters of the lateral columns in the sixth lumbar segment, and within the dorsal half in the seventh, and that they may still be largely in the lateral columns in the first sacral segment.

The operation of division of one pelvic nerve in the cat is not uncommonly followed by the presence of a significant volume of residual urine which can persist at any rate for several weeks. Since this result is not only not constant but does not even occur in the majority of cases, it seems probable that it is not due to division of nerve-fibres but to some other effect of the operation.

The only probable way in which residual urine might result from an unintentional lesion made at the operation is by stretching the remaining pelvic nerve in retracting the rectum. Against this being the cause of the residual urine is the fact that signs of paralysis of these nerves do not occur in acute experiments where both nerves have been exposed in the way used in survival experiments and not divided. To whatever cause this residual urine is due its importance for the present purpose is that when it follows a combination of division of one pelvic nerve with another lesion, the possibility of its being due to division of the pelvic nerve alone must always be excluded before assuming it is due to the combination. This can be done by dividing the nerve and seeing if residual urine follows before making the other lesion.

In one cat the right pelvic nerve was divided and no residual urine followed. In eleven days a lesion was made in the first lumbar segment which destroyed the whole of the right side of the cord except a small part of the periphery of the ventral column, together with the internal and dorsal sides of the dorsal column and the central grey matter on the left side. Residual urine followed and persisted for nine days but had disappeared in twenty-one days. In a second cat the left pelvic nerve was divided and a residual urine of 5 to 10 c.c. followed, the volume passed at each micturition being usually about 50 c.c. On the nineteenth day a lesion was made in the last thoracic segment which destroyed the whole of the right side of the cord except the ventral column, together with the dorsal column, the central grey matter and the internal part of the dorsal grey horn on the left side. There was a transient increase in the volume of residual urine which disappeared between the seventh and twenty-second days. In a third cat a lesion was made in the adjacent parts of the second and third lumbar segments, destroying rather more than the dorsal half of the right lateral column for more than half its thickness from the periphery inwards. The left pelvic nerve was divided twenty days later and no residual urine followed. In a fourth cat the left pelvic nerve was divided and no residual urine followed. In fourteen days a lesion was made in the adjacent parts of the second and third lumbar segments which destroyed the lateral column, the dorsal grey horn and the external part of the ventral grey horn on the right side. Residual urine followed but had disappeared in eighteen days.

From these four experiments it follows that there is an extensive but incomplete crossing of both the centrifugal and centripetal paths between the anterior lumbar region and the origin of the pelvic nerves.

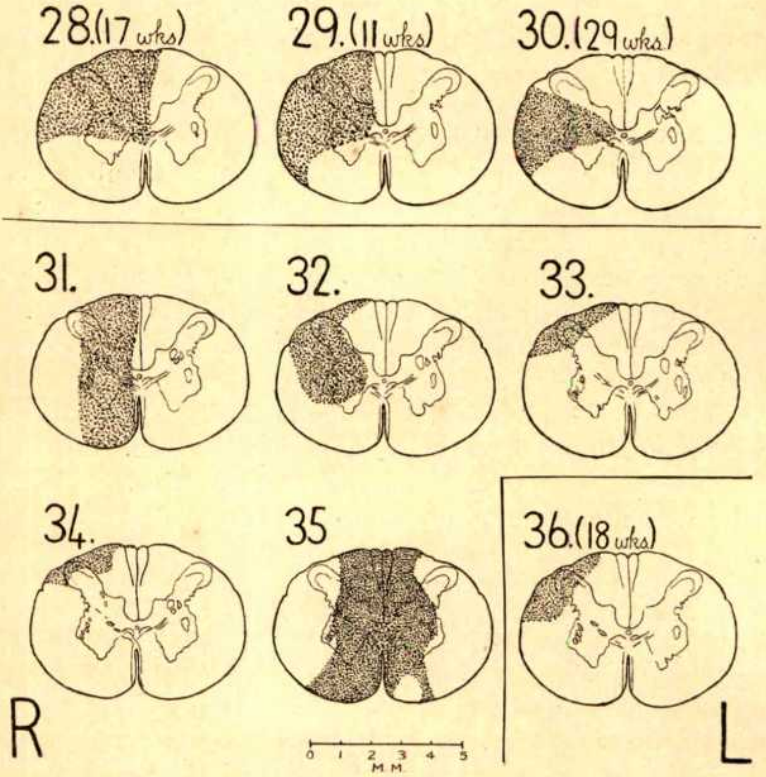
The level of this crossing can be determined by making a unilateral lesion in the anterior lumbar region involving at least the peripheral fourth of the dorsal half of the lateral column, combined with a similarly situated contralateral lesion further back, and observing how far back the latter can be made and be followed by both the defects in micturition which follow similar bilateral lesions in the anterior lumbar region. It can also be determined by dividing one pelvic nerve and subsequently making a contralateral hemisection and observing how far back the latter can be without being followed by any, or any additional, defect in micturition.

No. 22 shows that the crossing must be behind the sixth lumbar segment. The same results as those of No. 22 followed in a cat when the posterior lesion was in the seventh lumbar segment and they lasted twenty-eight weeks, when the cat was killed. In a third experiment with the same results, in which observations were made for twenty-two weeks, the posterior lesion was in both the seventh lumbar and first sacral segments, and at its maximum was a complete hemisection except for a thin strip of the ventral column along the ventral median fissure; the pelvic nerves were found by dissection to arise from the second and third sacral nerves, the branch from the second being the larger. This method therefore shows that the crossing must take place in the segments from which the pelvic nerve arises.

The same result is given by the second method. Three experiments were made, the left pelvic nerve being divided in each. In one after four weeks there was a small volume of residual urine. A lesion was then made which involved the dorsal horn, the external part of the dorsal column and the dorsal half of the lateral column on the right side in the fourth and fifth lumbar segments, without any increase in the residual urine following. In the second there was no residual urine and a lesion in the first sacral segment involving the whole right side of the cord and the central grey matter and internal part of the dorsal column on the left side was followed by residual urine which disappeared after twenty-two days. The right pelvic nerve arose by a large branch from the second sacral nerve, a smaller one from the first and a very fine one from the third. In the third experiment there was no residual urine and a lesion in the seventh lumbar segment involving the whole of the right side of the cord together with the greater part of the left dorsal column and adjacent grey matter was followed by the intermittent occurrence of a small volume of residual urine up to the sixty-second day, but not after. The right pelvic nerve arose by a large branch from the second sacral root, one about a quarter of the size from the first and a smaller one still from the third.

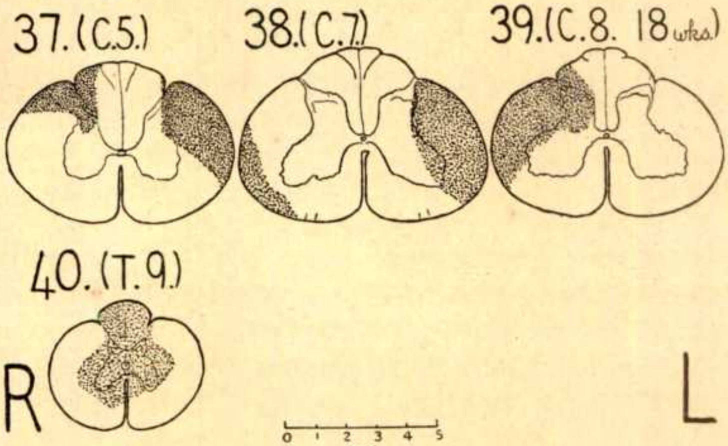
## VI.—THE CERVICAL AND THORACIC REGIONS.

A lesion of the periphery of the dorsal half of one lateral column, which involves at least a fourth of its thickness in the anterior lumbar region, combined with a lesion in the first cervical segment on the opposite side, may result in the presence of residual urine and loss of consciousness of a need to micturate. In two cats such a lesion in the anterior lumbar region was combined with a lesion on the same side in the first cervical segment. In one cat this lesion was a hemisection and in the other only a thin medial strip of the dorsal column, grey matter and ventral column escaped: neither cat developed residual urine. Three similar experiments were made with the same result, the anterior lesion being in the first, the sixth and the seventh thoracic segments respectively. In all three a small part of the homolateral ventral column escaped destruction, and in the case of the sixth thoracic a small medial part of the dorsal column in addition. There is therefore



no crossing of either path in the cervical or thoracic regions unless it is insufficient in degree to escape detection by the present methods.

Figs. 28 to 36 show the position and extent of lesions in the first cervical segment of each of nine cats. In each case the lesion was combined with one on the left, or contralateral, side in anterior lumbar region, or in the case of No. 36 in third lumbar segment, which involved at least the dorsal half of the lateral column for one-fourth of its thickness from the periphery. The number of weeks indicated after the number of the figure is the period for which observations were made after the second of the two operations. Nos. 28, 29 and 30 had residual urine and were unconscious of a need to micturate, Nos. 31 to 35 had no objective defect in micturition at the time they were killed, and No. 36 constantly had a small volume of residual urine but was conscious of needing to micturate.



Attempts to make a narrow lesion involving the dorsal half of the periphery of the lateral column always resulted in the formation of a deep one, apparently by infarction. In consequence of this the three positive experiments, Nos. 28 to 30, only show that both paths must be in some part of the dorsal half of the lateral column or in the wedge-shaped area of grey matter subtended by this towards the central canal. In four out of six cats in which retention was produced by a lesion in the first cervical segment on one side followed by one in the anterior lumbar region on the other, the urethral resistance was low when overflow first occurred. In other respects the micturition defects in Nos. 28, 29 and 30 were identical with those already described resulting from bilateral lesions in the anterior lumbar lesion, and these cats were also unconscious of needing to defæcate.

In numbers 31 to 36 retention did not occur. There was no residual urine in Nos. 31 to 35, but there was in No. 36. There was no loss of consciousness of the need to micturate in Nos. 31, 32, 35 or 36: observations on this point were not made in Nos. 33 and 34. It will be seen from the diagrams that more than the dorsal fourth of the periphery of the lateral column has to be destroyed before residual urine results, and that more than the deep half of the dorsal half of the lateral column can be destroyed without any residual urine resulting.

Nos. 37 to 40 show the position and extent of lesions in four of the remaining segments of the cord in each of four cats. In No. 39 there was also a lesion in the first lumbar segment on the left or opposite side which involved the periphery of the dorsal half of the lateral column: the cat had residual urine and was unconscious of needing to micturate. Nos. 37, 38 and 40 had no residual urine.

## Conclusions.

The centrifugal and centripetal paths of micturition undergo extensive crossing in the segments from which the pelvic nerves arise and possibly in the segment next in front of these. From then forwards there is either no crossing or it is insufficient to be detected by the methods used. Both paths are situated in the dorsal half of the lateral column near its periphery.

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# ON THE PHYSIOLOGY OF MICTURITION.

BY D. DENNY-BROWN AND E. GRAEME ROBERTSON.

*(From the National Hospital for Nervous Diseases, Queen Square, London.)*

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## (1) INTRODUCTION.

MOSSO and PELLACANI, in 1882, when the method of making continuous smoke-drum records had just been introduced by Marey, described a series of experiments upon the normal female human bladder [18]. Their method was highly ingenious, and consisted of running records of the movements of a vessel of which the fluid contents communicated by tube and catheter with the interior of the bladder. The level of the fluid was kept constantly slightly above the level of the bladder and the record was therefore of variations of vesical volume at constant pressure. They described and figured slow fluctuations of vesical volume occurring at times spontaneously and at times in response to attempts to micturate. They were especially concerned to eliminate change of abdominal pressure, or variation of blood-pressure as a cause of these fluctuations. The fluctuations of volume were interpreted as active vesical contractions. Similar fluctuations were found to occur when the subject exerted emotional or intellectual effort, and the function of the organ was therefore considered to be closely related to the intensity of psychological processes. Introduction of an additional volume of fluid revealed a subsequent adaptation of the bladder to its contents, provided the immediate reaction to introduction was allowed to subside, so that the pressure within the organ gave little or no indication of the volume it contained. It was concluded that desire for micturition was stimulated when the pressure rose above 18 cm. of water, and was not directly related to volume.

Subsequent observations upon the human bladder by many authors, made by measuring at intervals the pressure of fluid by a water manometer connected to a catheter, confirmed the process of adaptation to a mean pressure which rises little as volume increases over a moderate range. Sooner or later a volume is reached at which an active vesical contraction occurs and fluid is ejected from the bladder at high pressure (Rehfisch [21], Schwarz [24], Dennig [6], Adler [1]). Records of vesical pressure obtained by this means tended to belittle and indeed disclaim any rhythmical contractile activity in the human bladder (Dennig [6]).

Rehfisch [21] observed that even if the external, voluntary sphincter were held open by a catheter the vesical contents were retained by the internal involuntary sphincter which embraces the most proximal urethra. He stated that micturition could be commenced voluntarily under these conditions and maintained, therefore, that the internal sphincter relaxed by effort of will. Boeminghaus [5], by means of X-rays of the bladder filled with opaque solution, demonstrated that the internal sphincter is normally completely closed until micturition occurs. He also observed that after prostatectomy, by methods which destroyed the internal sphincter, urine was still retained by involuntary activity of the external sphincter. Young [29] devised an instrument to dilate the internal sphincter while allowing the external sphincter opportunity to close, and found that urine could be held comfortably by the external sphincter. There is therefore some evidence that both sphincters can function involuntarily in retaining the contents of the viscus. The manner and degree of ability to relax these two sphincters and the manner in which voluntary and involuntary closure is brought about has remained in doubt.

Rehfisch [21] found, by introducing a catheter of fine calibre into the bladder and measuring vesical pressure by a manometer tube, that a large rise of pressure occurs during micturition. The relationship of this vesical contraction to the onset of micturition and the mode of transition of involuntary adaptation of the bladder to active micturition remained matters of speculation.

The extensive researches of Mosso and Pellacani [18], von Zeissl [32], Rehfisch [21], Sherrington [26], Elliott [8], Barrington [3, 4] and others into the innervation of the bladder upon animals has been admirably reviewed by Fearnsides [9] and Barrington [3], and more recently by Dennig [6] and Adler [1]. Of the two pairs of nerves reaching the vesical plexus, the sacral (parasympathetic) nerves, derived from the sacral plexus, when stimulated relax the internal sphincter and contract the detrusor musculature of the vesical wall. The "hypogastric" nerves derived from the sympathetic chain on each side via the inferior mesenteric ganglion, have in general the reverse effect· The effect of stimulation of this nerve upon the internal sphincter and trigone in man has recently been described by Learmonth [17]. Section of the hypogastric nerves has been followed only by slight frequency of micturition, a finding which suggests more function by the remaining sacral nerve supply in regulating adaptation to volume than the effect of its stimulation would indicate. The external or voluntary sphincter, innervated by the pudic nerve, appears to have little part in the initiation or completion of micturition, but the researches of Barrington [4] reveal some slight but constant incontinence following the section of this nerve in animals. It has been stated that there is no voluntary sphincter in the female urethra and that this sphincter plays no essential part in micturition, but Zangenmeister [31] describes and pictures sufficient voluntary muscle situated around the proximal female urethra to refute this statement. Goltz [11], from observations on micturition in the spinal animal, put forward the view that spontaneous contractions of the bladder caused the expression of some drops of urine into the posterior urethra, with consequent desire for micturition and completion of the act. The series of reflexes described by Barrington [4] would appear to provide the mechanism for the completion of the process. Guyon [12], however, showed that distension or irrigation of this proximal part of the urethra in man had no demonstrable effect in facilitating micturition or in stimulating desire to micturate.

Most authors except Rehfisch [21], Adler [1] and Le Gros Clarke [16] are unwilling to allow the possibility of any direct voluntary control over the smooth muscle of the bladder and internal sphincter. Müller [19] seeks to avoid this implication by suggesting a reflex control of the bladder by afferent impulses arising in the voluntary external sphincter, and thus willed effort to micturate would affect the bladder indirectly. Schwarz [24] obtained records of vesical pressure by means of a fine catheter and manometer, and noted the relationship of the onset and termination of micturition as it occurred around the catheter. Both Schwarz and Rehfisch maintain that a rise of vesical pressure is the primary event in voluntary micturition. Their methods, however, do not give information as to the part played by the internal sphincter in the initiation of the act. Adler [1, 2] holds that the primary event is relaxation of the internal sphincter with subsequent reflex relaxation of the external sphincter and vesical contraction. The effective performance of micturition after prostatectomy with excision of the internal sphincter and prostatic urethra seems to indicate that these structures play no very necessary part in the initiation of the act.

Considerable variation in opinion therefore exists as to the sequence of events in normal human micturition. In the course of some work on the disturbances of micturition by nervous diseases we have developed a technique for obtaining continuous records of vesical pressure during manipulations of the volume of the bladder. In the control experiments upon normal subjects we have accumulated some data bearing on the sequence of events in normal micturition and their control, and present them here, together with a description of the method we have employed.

## (2) METHOD.

The method of recording vesical and urethral pressure which has been used has developed in the course of a study of the disturbances of micturition in twenty-five cases of nervous diseases. The present work is based upon seven prolonged experiments on three male subjects, all of whom were in perfect health, except that Subject C was a patient suffering from a chronic retinal condition. In no subject was there reason to believe that micturition was or ever had been in any way abnormal.

With aseptic precautions the subject of the experiment is catheterized with a soft rubber catheter of moderate size and having its proximal aperture situated at the tip. Through this catheter is passed an ordinary ureteric catheter of small outside diameter. No anæsthetic was used in any of the experiments. The distal extremities of the two catheters are attached to a sterile glass adapter arranged as in fig. 1 B, so that the small ureteric catheter *b* gained exit from the space connected with the lumen of the rubber catheter *a*, by a small rubber cork *d*. The ureteric catheter was led to a small glass adapter *e*, to which it was attached so that its lumen communicated with the interior of the adapter. The glass adapters each contained a pressure chamber *f* and *l*. The fluid was allowed to reach a level in each pressure chamber; on changes of pressure in the interior of the catheters the fluid level rose or fell independently in the two pressure chambers.

The pressure within the pressure chambers was transmitted by air in thick-walled rubber tubing *g* and *m*, to the interior of two manometers, each consisting of a small glass funnel, as is shown in fig. 1 A *o*, over the mouth of which is stretched stout rubber sheeting *p*, which is fixed by wire binding at the lip of the funnel. As the rubber membrane has to withstand pressures of over 200 cm. of water, the rubber must be of such strength that it bulges only about a millimetre at this pressure, and the joint between rubber and glass is sealed by varnish ("gold size" was found most suitable) so that the system is completely air-tight. To one side of the rubber diaphragm is attached by varnish a small mirror of polished stainless steel with an optically flat surface *q*. The manometers are fixed in adjustable clamps so that each may be adjusted independently, and are attached to an upright steel pillar set in a

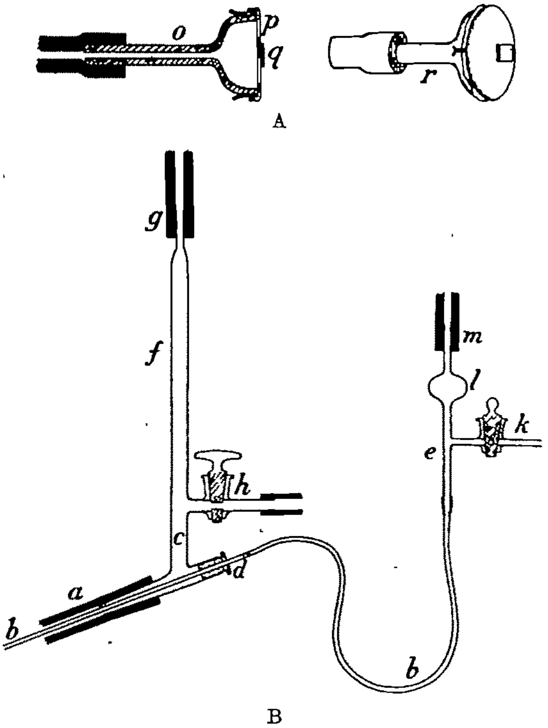

FIG. 1.—Diagrammatic section of the apparatus used to register the pressure within the catheters. Fig. 1 A shows the construction of the mirror manometer used; B shows the connections of the two catheters, *a* and *b*, with the glass adapters which serve to transmit the pressure in each to the appropriate manometer. The details are explained in the text.

cement floor so firmly that no ordinary movement on the floor caused in them any evidence of vibration.

Change of air pressure within the manometer, transmitted from its pressure chamber by some 60 cm. of rubber tubing, caused equivalent fluctuation of the diaphragm and consequent swinging of the steel mirror through a slight angle. A beam of light passing through a narrow slit is thrown upon the mirrors and by them reflected at an angle to fall upon the slit of a moving paper camera situated 2·2 metres from the manometers. As a continuous strip of bromide paper, 7·5 cm. in width, moves in the camera past the slit the reflected beam of light traces the fluctuations of the mirrors with high magnification. A revolving Rayleigh electrical time marker interrupts a steady beam of light on the edge of the paper so that a continuous series of fine vertical strokes are made at $\frac{1}{5}$ sec. intervals. The shadows of two electromagnetically operated signals are arranged to fall upon the camera slit and thus record their movement upon the paper. By operating a switch a movement of one or other can be made at will. Three other manometers, similar to those for the catheter pressure chambers, were used to record the movements of the abdominal wall, the pressure within the rectum, and the movements of the perineum by means of small rubber balloons attached to thick walled rubber tubing. These were moderately distended, and the abdominal and perineal balloons were placed under binders which held them applied to the umbilicus and over the M. bulbocavernosus respectively. The rectal balloon was some 3 cm. in diameter when fully distended and was introduced, well lubricated by soap, into the rectum where it was slightly inflated by introducing some air into a side tube of the manometer.

The subject lay supine upon a couch and was provided with an electrical key by which he could signal any events he wished upon the camera paper. The lower limbs were slightly flexed and abducted, and an upright supported the two glass adapters so that they were conveniently near the penis.

To each glass adapter, in the lower part of the pressure chamber, a side tube with tap (fig. 1 B *h* and *k*) is arranged, and to either can be attached a length of rubber tubing leading to a reservoir graduated in cubic centimetres and containing a thermometer. The reservoir was of moderate capacity, 600 c.c., so that it could be readily raised and lowered by hand. With the disposition of catheters shown in fig. 2 A the reservoir was connected to *h*, with that in fig. 2 B, C, D, to *k*.

The pressure at which the fluid was introduced into or removed from the bladder was measured by arranging a vertical scale graduated in centimetres alongside the couch, with the zero corresponding to the level of the symphysis pubis. Fluids were usually introduced by the tap *h* (fig. 1) so that the manometer *f* attached to the pressure chamber recorded during introduction a pressure which was a resultant between the vesical pressure and the reservoir pressure. When the tap *h* was closed this manometer recorded vesical pressure alone. The other manometer, attached to the pressure chamber *l*, would continue to record true vesical pressure whatever the fluctuations taking place in *f*. In order to keep the pressure of input of fluid constant the reservoir was held by hand next the vertical scale so that its fluid level remained constantly opposite the required height. A mechanical arrangement for this purpose was found unsatisfactory owing to the unavoidable friction of pulleys.

Fluctuations of pressure were readily and accurately revealed by the manometer attached to the pressure chamber *f*, owing to the wide communication it maintained with the interior of the urethra. The ureteric catheter *b*, on account of its narrow internal diameter, offers some resistance to movement of fluid rapidly in either direction. A slight fluid impact at the tip of the catheters was found to be transmitted to the manometer attached to the small ureteric catheter with a latency of some 0·01 sec., and to the manometer attached to the rubber catheter rather more slowly, about 0·015 sec., owing to the greater resiliency of the rubber. The movement of fluid commenced to record after a slightly longer interval in each, so that for the commencement of change of pressure the narrow lumen of the small catheter offered no recognizable error at our speed of recording. With changes of pressure of over 100 cm. water in intervals of less than three or four seconds the manometer of the small catheter showed some lag in reaching final values, but as such changes were rarely our experience the error is negligible, and when it occurs in the records it is indicated. Lagging of pressure changes owing to obstruction of the openings of the catheters by folds of mucous membrane tended to occur when the volume of the bladder was very small. The flat curves thus produced are readily recognizable. The high tension of the rubber diaphragm of the manometers, the lightness of the mirrors, and the small amplitude of movement ensured that the vibration frequency was of very high order, and no allowance need be made for overfling or vibration from this cause.

In order to avoid the confusion of too many parallel deflections the excursion of two of the manometer images, those of the abdominal and rectal recorders, were arranged to show a downward deflection for rise of pressure, the others to show an upward deflection.

Dubois [7] pointed out that vesical pressures taken from the level of the symphysis pubis as zero show difference from pressure at the actual centre of the bladder. The error is slight and is a positive value with an empty bladder and negative with the distended bladder. The values given here are uncorrected and thus should be comparable to those of Mosso and Pellacani, and most later workers. The symphysis pubis is much the most convenient base line for use in clinical work with abnormal bladders. In practice the catheters are passed, the bladder emptied by placing the reservoir at a negative pressure of – 20 cm. water, the pressure chambers of the glass adaptors are filled to a convenient level, and with the reservoir held with its fluid level corresponding to that of the symphysis pubis the manometer images are

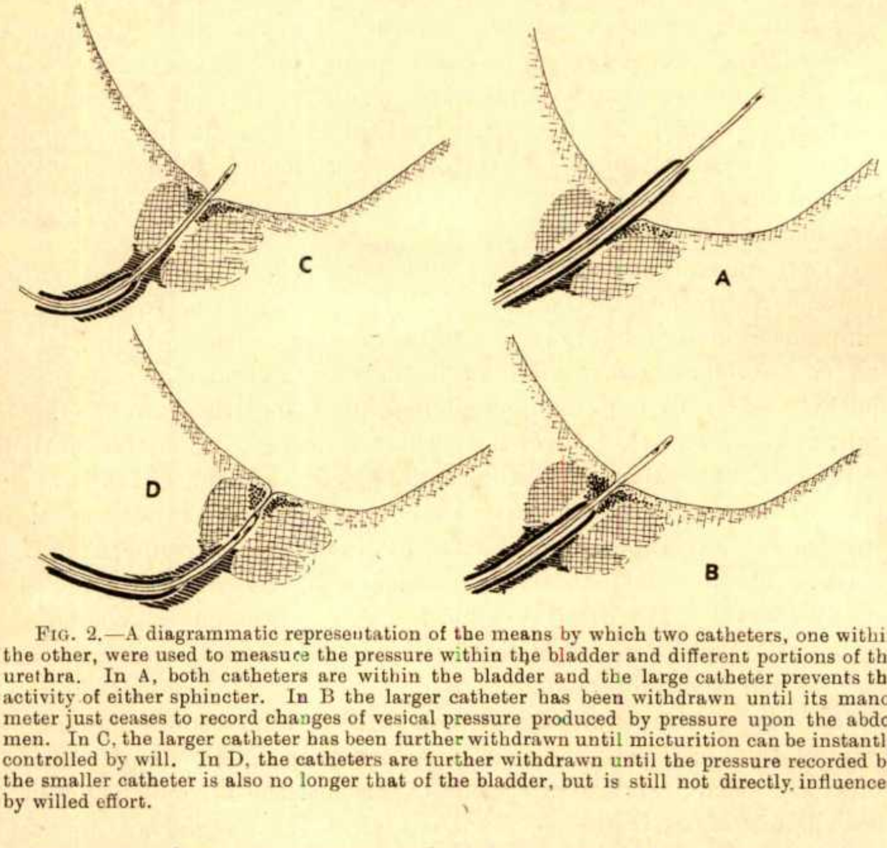

FIG. 2.—A diagrammatic representation of the means by which two catheters, one within the other, were used to measure the pressure within the bladder and different portions of the urethra. In A, both catheters are within the bladder and the large catheter prevents the activity of either sphincter. In B the larger catheter has been withdrawn until its manometer just ceases to record changes of vesical pressure produced by pressure upon the abdomen. In C, the larger catheter has been further withdrawn until micturition can be instantly controlled by will. In D, the catheters are further withdrawn until the pressure recorded by the smaller catheter is also no longer that of the bladder, but is still not directly influenced by willed effort.

adjusted to fall on the base line of the moving bromide paper, before recording was commenced. The fluid used was sterile normal saline at reservoir temperatures of from 115° to 105° F.

Manipulation of the catheters secures variable disposition of their opening within the bladder and urethra, which are shown diagrammatically in fig. 2. The use of these dispositions is explained below. It was found that to maintain the dispositions shown in fig. 2 B, C, D, constant the catheters should be firmly held by the gloved hand of the assistant, otherwise they tended to move outwards during micturition.

When the outlets of the system are closed, any contraction of the muscle of the wall of the bladder occurs under conditions of almost constant length of muscle fibre, a type of contraction called for convenience "isometric" contraction. With varying freedom of outflow the type of contraction has a variable isotonic property, though with this method no true isotonic contraction can be obtained. The advantage of the isometric record of any muscular contraction is the avoidance of distortion due to shortening, more cleanly cut relaxations, and more direct relationship between height of record and quantity of contraction.

### (3) THE REACTION TO DISTENSION.

The behaviour of the bladder during distension was similar in each of the three subjects. Our usual procedure was to allow fluid to enter the bladder through a narrowed aperture and under a constant pressure of 50 cm. water. The inflow was closed for an interval after the entry of each 100 c.c. in order that the vesical pressure could be observed under approximately isometric conditions. As each 100 c.c. of fluid was allowed to enter the vesical pressure rose gradually, to reach from 2·5 to 7·5 cm. water pressure at 100 c.c., and with gradual increments of volume reaching a pressure of approximately 10 cm. water at 500 to 600 c.c. (fig. 3 and Plates I, II). From that volume onwards the pressure rose more steeply to 18 to 20 cm. at 675 to 700 cm. (two subjects, Subject C not subjected to such high volumes). A slight fall of pressure during the intervals of rest at constant volumes under isometric conditions indicates the occurrence of a process of adaptation, a readjustment of vesical tension. This adaptation was definitely greater at higher volumes, and contrary to the conception of Mosso and Pellacani [18] was not in the nature of an adjustment to an almost constant tension of approximately 15 cm. of water but rather approaching a percentage adaptation of the tension induced by the previous filling. The graphs

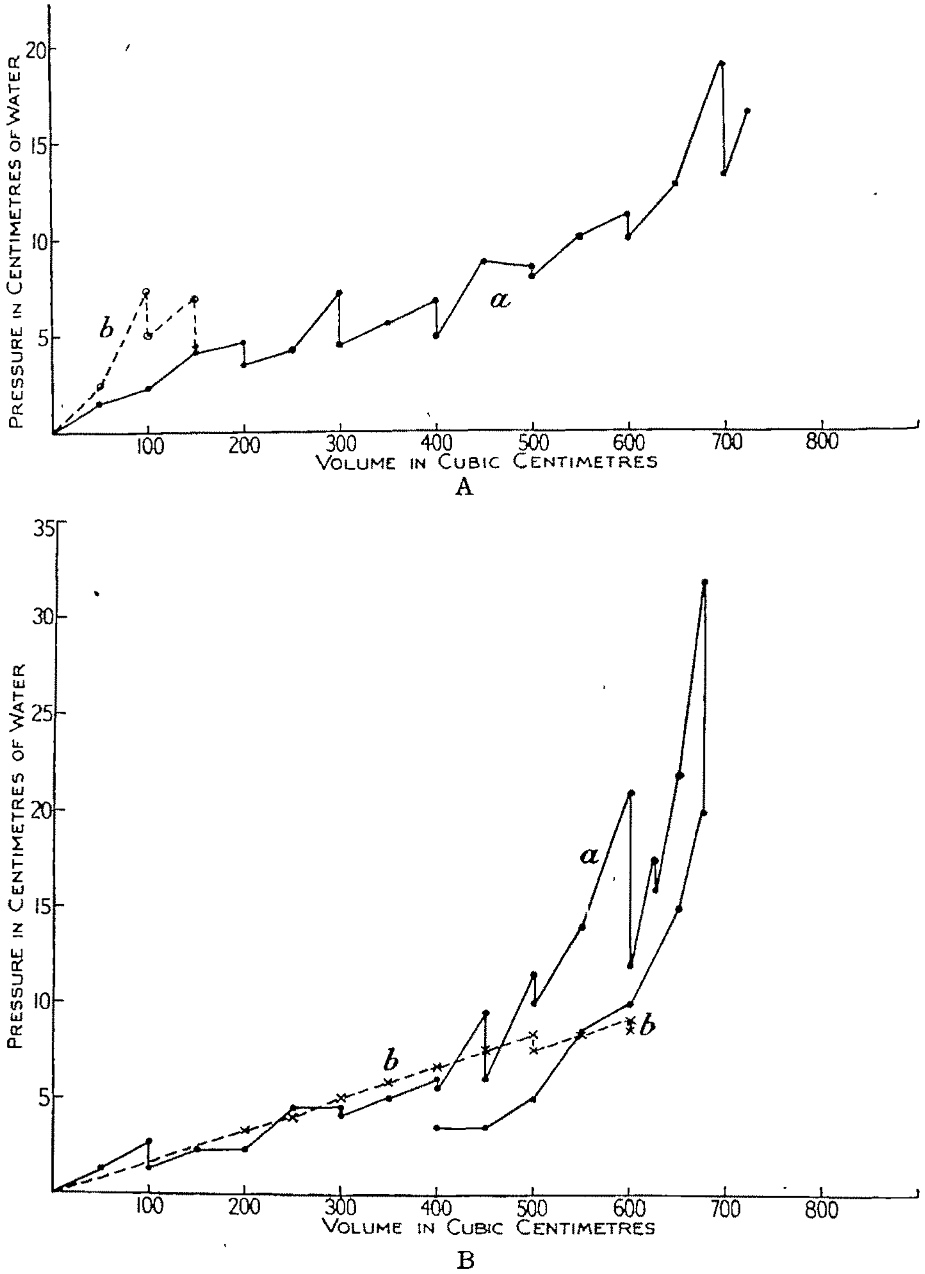

FIG. 8.—Graphs of the relationship of the volume of the vesical contents to their pressure in the course of distension of the bladder. Fig. 8 A shows two curves obtained from subject A. The continuous line *a* is from data from the record shown in Plate I. The short curve *b* is from another experiment. The curves in fig. 1 B are from two experiments on subject B; the continuous line *a* is from the record of the filling shown in Plate II; *b* is from a later experiment, where the bladder had been very distended for some time before this filling. Each vertical fall of pressure indicates the degree of adaptation at a constant volume.

shown in fig. 3 reveal the variability of degree of relaxation of the tension exerted by the vesical wall following cessation of filling at different volumes. It will be seen from the graphs that resting vesical tension at moderate volumes varied from 5 to 10 cm. of water, and we have come to regard this range as the normal pressure of vesical contents. Acceleration of rate of filling increases the reactionary rise of tension, but, providing that attempted micturition does not occur, the pressure is still below 10 cm. at moderate volumes and the final adaptation reaches a pressure commensurate with the resting pressure for equal volume during slower filling. A *sudden* passive distension of the bladder often occasions a small reactionary wave (Plate III, fig. 3).

Adaptation of this degree necessarily implies the presence of a process of active vesical contraction before the adaptation occurs, for the bladder of the cadaver shows only a visco-elastic reaction (Osborne [20]). The argument is in fact exactly parallel to that by which the stretch reflex of voluntary muscle is demonstrated experimentally.

Distension of any viscus within the abdomen raises the intra-abdominal pressure. The muscles of the abdominal wall make an adaptation of their posture to changes of intra-abdominal pressure (Kelling [15]), and the effect of this adaptation is necessarily reflected and added to any adaptation made by the bladder. The extent of adaptation occurring in the experiments at present described may be gauged by the very slight changes reflected by intrarectal pressure (Plates I and II). The moderate speed and degree of adaptation therefore point to the existence of a mild tonic vesical contraction, induced by the process of distension, varying in degree with the rate of distension, and fading when distension ceases.

It will be noted that according to the shape of the curves the degree of this tonic contraction differs not only from subject to subject at comparable volumes, but also differs in the same subject at different times. For example, in fig. 3 B, *a*, the vesical tensions at volumes of from 400 to 675 c.c. were much higher during increasing volume than during emptying. Similarly in another experiment when the bladder had been distended for some time before the experiment by a volume of 827 c.c., a record of filling (fig. 3 B, *b*) shows volumes approaching those of the previous emptying shown in fig. 3 B, *a*. The curve in fig. 3 B, *b*, takes a rectilinear course which would appear to imply complete absence of any reaction, and must approximate to the curve of a completely paralysed bladder. This finding is in complete accord with Mosso and Pellacani's statement [18], that if the bladder has been very distended the tonic reaction at smaller volumes is for a time lessened.

There are certain exceptions to this mild reactive process. In Subject A, at or just below the volume of 100 c.c., and again at irregular periods (e.g., at volumes of 300, 450 c.c.), the resulting value of vesical tension showed regular fluctuations (Plate I). These waves of pressure appeared during filling; they were more frequent at the cessation of a filling, and gradually lessened in amplitude to complete disappearance. Rarely there was a single such fluctuation, as at a volume of 300 c.c. in Plate I. They were not accompanied by any sensation at moderate volumes, and appeared without the subject's knowledge. They were not directly related to the degree of vesical reaction provoked, as judged by the pressure immediately preceding or following the wave-like fluctuations.

The gradual rise in vesical tension as filling proceeds does not, at low volumes, intrude upon the consciousness of the subject. Introspection fails to bring any feature into conscious appreciation. We shall discuss later the sensations derived from distension at higher volumes.

In Subject A at a time when the vesical contents had reached 725 c.c. the pressure rose steeply in a wave to a crest pressure of 48 cm. (Plate I, *d*). This was accompanied by a sensation of increasing discomfort, so that the subject immediately exerted an effort to "hold water" by a voluntary contraction of the perineum and a strong-willed effort to postpone the sense of imminent micturition which formed a prominent feature of the accompanying compound sensation of discomfort. The rapid decline and disappearance of this wave disturbance was therefore possible evidence of its subjugation by an effort of will. That this had indeed taken place is further suggested by the recurrence of rising pressure soon after the subject had signalled that, the discomfort having in greater part vanished, the voluntary effort to overcome it was relaxed. There then occurred a disturbance reaching a high pressure (Plate I, *e*, *f*) which, though at first slightly modified by effort of will, proceeded to violent and painful vesical contraction which ceased only when a considerable volume of fluid had been expelled from the bladder.

In the Subject A there therefore resulted, as a consequence of continued distention of the bladder, a reaction which though at first modifiable by will had eventually the appearance and effect of an involuntary expression of vesical contents. The development of this process shows grades of transition from the mild wave disturbances observed during filling.

In one experiment on Subject B similar small fluctuations appeared at times, usually as in Subject A, towards the termination of a period of filling (Plate II, after B, O, and *e*), but they were less clearly uncomplicated by movement of the abdominal wall. Although filling in this subject was carried on to a volume of 675 c.c. no vesical contraction reaching a high pressure occurred. Extreme discomfort experienced at this volume led us to abandon further filling. In Subject C the volume was not taken higher than 400 c.c. and no wave-like fluctuations of pressure were observed. We wished to spare this subject the possibility of discomfort and higher volumes were avoided.

## (4) MODIFICATIONS OF VESICAL PRESSURE INDUCED BY WILLED EFFORT.

While the mild reaction of the bladder to filling at moderate volumes is accompanied by small waves of pressure without the knowledge, wish or consciousness of the subject, a willed effort to micturate may have a very definite effect. Subject B, when the bladder had been filled to a volume of 200 c.c. and with the system closed so that the volume remained constant, made a prolonged effort to micturate. This effort (Plate III, fig. 1) was in the nature of a relaxation of the perineum, with slightly increased tension of the abdominal wall. The immediate effect of this procedure was a slight fall in vesical pressure, presumably reflecting the fall in intra-abdominal pressure induced by relaxation of the perineum. After some thirty seconds the vesical pressure rose slowly and evenly to 30 cm. of water. The subject was then instructed to "hold hard" and to attempt to overcome micturition. The vesical pressure progressively declined to resting value, showing an acceleration after cessation of the effort to restrain. This acceleration of fall appears to be related directly to the relaxation of the perineum, and is interpreted as evidence that the tightening of the perineal diaphragm during the period of restraint had induced a small passive increase of intra-abdominal pressure which had corresponded with the falling vesical pressure.

The voluntary effort made by the subject in the attempt to micturate involves relaxation of the voluntary musculature of the perineum, and the subject himself is aware of the process primarily in a sensation derived from the perineal region. The manœuvre is introspectively that of letting go some faint holding of the perineum. The "holding" is not itself conscious except faintly by introspection, and the recorder of perineal movement reveals that the perineum continues to hold the same posture whether the subject be thinking of it or has his attention directed elsewhere for long periods. The differentiation from a "strain" is important. If the subject be instructed to attempt to initiate micturition by "bearing down" the recorded events are altogether different. Such a strain in this subject produced only a progressive rise of vesical pressure in direct proportion to the amount of increase in abdominal pressure secondary to contraction of the abdominal wall and diaphragm (Plate II, F, G, H, and I). The perineum also contracted in some efforts (Plate II, *b*). A strain may be made mainly by diaphragmatic movement (Plate III, fig. 6, C). There is no independent change of vesical pressure.

The rise of vesical pressure in response to voluntary effort more commonly exhibits a fusion of waves. This type of facilitation is shown in Plate III, fig. 2, where no change in movement of the abdominal wall accompanies the development of vesical contraction. The vesical pressure is heightened in waves of increasing amplitude which fuse to form a plateau at 50 cm. pressure. A voluntary effort to overcome the disturbance resulted in a progressive fall of tension, commencing on this occasion four seconds after the abrupt movement of the perineal recorder indicated the onset of the perineal "holding" movement. A wave of pressure which commences just before the onset of the perineal contraction appears to run its course before relaxation commences. There is some slight undulation upon the decline of tension.

In Subject A the facilitation of appearance of waves of increased pressure was even more striking. In one experiment the amplitude and frequency of waves was directly proportional to the degree of voluntary effort to micturate. Thus, at a volume of only 100 c.c., when the subject was resting comfortably, but making a slight conscious effort to postpone a desire for micturition (which in this case followed a powerful contraction of the bladder induced a minute or two earlier) the vesical pressure remained very low, without spontaneous waves, and the perineum was contracted to a slight but definite degree. When the subject consciously relaxed the perineum and contracted the abdominal wall slightly, but determined that he should not encourage micturition (Plate III, fig. 4) the pressure rose slightly and a slight rhythmic fluctuation became evident. If the subject then thought of micturition and allowed sufficient relaxation of the perineum to cause a feeling that micturition was possible, but determined not to relax further, the pressure showed a series of regular waves reaching 20 cm. pressure at about twenty seconds interval (Plate III, fig. 5). These waves gradually lessened in amplitude and the condition reverted to the previous state.

If the subject encouraged such a desire for micturition by a full relaxation (still avoiding any active effort to express urine) a large wave of pressure develops with surprisingly short latency and requires sudden and intense voluntary conquest by "holding" to prevent its development into a painful spasm (Plate III, fig. 5, B, C, D). This facilitation of vesical contraction, under isometric (constant volume) conditions, by a willed effort, develops shorter latency and greater amplitude with repetition, so that the interval before its commencement after an accurate signal of the onset of voluntary effort may be extremely brief (1·6 sec. measured from the first indication of perineal movement in

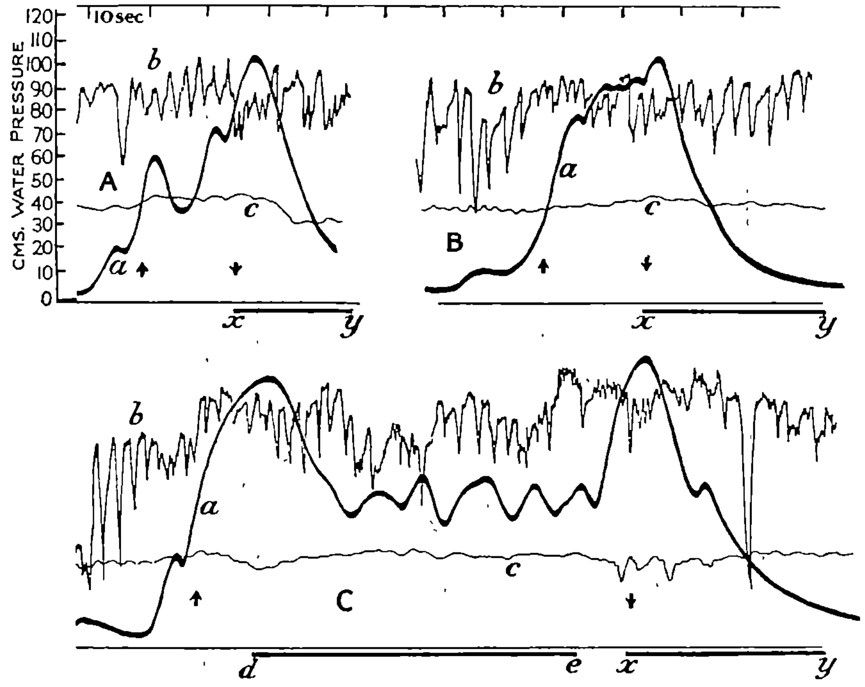

Fig. 4.—Three records of micturitions in response to voluntary effort, from a series obtained from Subject A during one experiment. The vesical pressure is shown by the heavy curve *a*, the movements of the abdominal wall by the irregular tracing *b*, and the changes of intra-rectal pressure by the curve *c*. The curves read from left to right. The vesical pressure is shown on the scale in cms. of water. The commencement of the rise of vesical pressure in each of the micturitions occurs in response to an effort commenced some seconds earlier. The occurrence of discharge from the sphincters (disposition as in fig. 2 C) is shown as a small arrow directed upwards. The abrupt cessation of discharge is indicated by an arrow directed downwards; it occurs in response to the onset of a powerful effort to restrain micturition made in the period *x*—*y*. In C, a less powerful effort to restrain, corresponding to the line *d*—*e*, does not secure complete closure of the sphincter, although it is accompanied by a rapid lessening of the vesical pressure and the appearance of rhythmic fluctuations.

Plate III, fig. 7 A). Some evidence of rhythmical waves in the course of a willed vesical response has been seen (Plate III, fig. 2). In a series of such responses all transitions are seen from simple waves, such as those in Plate III, fig. 6, to simple compounds (fig. 4 A in text, and Plate III, fig. 5 D, and 7 E), and varying degrees of fusion of plateaux (fig. 4 B). From smooth fused curves willed effort of restraint, when mild, has occasionally the surprising effect of throwing into relief a rhythmical substratum (fig. 4 C). Thus waves are dissected from more perfect compounds by the process of inhibition.

An isolated large vesical contraction induced by will is evidently a compound of small waves of moderate frequency (6 to 12 a minute). Mild facilitation will induce the appearance of such compounds in rhythmical series at a frequency of three to four a minute. It is not possible to determine from these experiments whether each wave in a compound is an expression of contraction of the same muscle fibres, but from the tensions developed it would seem necessary that this should be so. The muscle is thrown into virtually a tetanic contraction in which wave after wave fuses with its predecessor. We have seen such waves reach a tension of 260 cm. water. The smaller waves show marked resemblance to the single twitch of the bladder of the cat recorded by Stewart [27].

The conquest of large vesical contractions by an effort of will presents some features of unusual interest. In Subject A it was possible to record the effect of exertion of a maximal effort to overcome the contractions with different intervals of onset of that effort after commencement of the contraction wave. If the effort to overcome commences at the very onset of the wave of contraction the wave runs a regular sharp single peaked course, followed by a relaxation nearly as steep (Plate III, fig. 6 A). The commencement of the effort at any later moment up to just before the crest of the wave (Plate III, fig. 7 B) results in a wave of similar form and time relations. An effort exerted at the crest of the wave is too late to prevent the occurrence of a wave approximately double the size, presumably due to a second superadded wave which takes a course similar in time relations to the first wave, and already in course of development at the moment of onset of restraint (Plate III, fig. 6 E, 7 E, 6 *b* and 5 C). Large waves are often demonstrably compounds of smaller waves superimposed crest upon crest, though the ascent is at other times so steep that no fusion points can be detected. The effect of maximal voluntary effort to restrain is therefore eventual steep and complete relaxation if the effort is sustained, but it is apparent that once a single wave is in progress it cannot be cut short. The explanation for this varying latency may rest upon some peculiarity in the process of development of inhibition in the mechanism of rhythmical excitation, but we prefer the simpler provisional explanation based on the supposition that each wave represents a volley of discharge of nerve impulses into the vesical musculature. Once such a volley of discharge occurs the slow muscular contraction is inevitable, and not influenced by inhibition. There would appear no necessity to relate this powerful inhibitory effect to the feeble and altogether doubtful potentialities of the hypogastric nerve.

It may here be pertinent to emphasize that from its nature as a hollow organ of which the motor effect is directed upon its contents, it is an *a priori* necessity that if any contraction occur it should occur in every part of the wall at one moment. This is in fact readily observed in the animal bladder to be the case, for the organ, unlike the bowel, does not move over its contents, it contracts as a whole or relaxes as a whole, except under the artificial condition of stimulation of a nerve belonging to one side of it. It is therefore a legitimate conclusion as a first step in analysis that each wave of pressure of the contents of the organ represents an active contraction distributed evenly throughout the wall. Further, since vesical muscle is composed of discrete, entirely separate fibres, such a response, accurately timed to occur in them all, must necessarily be the result of an outgoing nervous impulse adequately co-ordinated in time in the effector neurones concerned. In the bladder isolated from its connections with the central nervous system feeble spontaneous contractions of the muscle can still be obtained (Stewart [27]), but are not co-ordinated. Any regularity of rhythm resembles then the beating of but a few fibres. For the purpose of the analysis of the present records therefore it is possible to conclude that the effect of voluntary facilitation of contraction of the urinary bladder is to throw into activity the spontaneous synchronous "beating" of the motor neurones lying in the vesical plexuses and wall of the bladder. The thickness of the vesical wall allows fluctuation in intensity of contraction both by variation in the number of layers or fibres taking part in the contraction, and also by variation in frequency of nerve impulses being discharged into the muscle fibres.

It is not within the scope of our experimental method to determine the precise mechanism of that smooth tonic contraction which results from moderate distension and which by its partial relaxation determines adaptation. We see no objection to the supposition that it is the result of the excitation of small groups of muscle fibres throughout the organ in such a way that some are always coming into contraction as others relax, a consequence of a continual "peppering" of impulses as has been conclusively demonstrated to occur in postural contraction of voluntary muscle. The effect of voluntary willed effort would appear therefore to be an enhancement of the wave form of co-ordination which occurs subconsciously and involuntarily, the acceleration of the rhythm of co-ordinated discharge and the facilitation of its spread to more and more of the muscular fibres. All these features are found in the graduations of spontaneous vesical contraction, from which therefore the willed contraction reveals no features of difference in form. Voluntary inhibition of the process gives evidence that with very brief latency all motor discharge to the bladder-wall is caused to cease, and after the preceding muscular contraction has run its course relaxation of vesical tension occurs.

### (5) THE MODIFICATION OF THE GENERAL REACTION TO FILLING BY VOLUNTARY REACTION.

Subject A, whose graph of filling pressures is shown in fig. 3 A, showed in his first experiment no large voluntary facilitations during filling and only a large involuntary response at the termination of filling. When, immediately following upon this, the bladder was refilled and the catheters now arranged as in fig. 2 *c*, so as to obtain records of sphincteric function, it was found that discharges could be obtained at such volumes and later at volumes as low as 50 c.c. The details of the response of the sphincters will be discussed below, and here it may be remarked that each response was accompanied by a large compound wave disturbance evoked by a process of relaxation (fig. 4). Abdominal contraction was practised many times without any evidence of its setting up any process of micturition (Plate III, fig. 6, and Plate IV, fig. 5) even when superimposed upon mild vesical contractions already in progress (Plate IV, fig. 7, at B). Subject C, a hospital patient, had, though very willing to help the investigation, no particular interest in the results obtained, and no particular power of introspection. He invariably responded to the order to try and pass urine by a strain upon the abdomen, as shown by the tightening of his abdominal wall, the rise of rectal pressure, slight bulging of the perineum and a linear rise of vesical pressure. This procedure was unsuccessful in setting up vesical contraction, and was equally unsuccessful in subjects A and B. Subjects A and B, having more direct interest in the investigation, had found by introspection of their own sensations from normal micturition that the primary process was always some relaxation of the perineum, and an imitation of this under experimental conditions formed the basis of the voluntary facilitation described above.

When Subject A was submitted to a second experimental filling at a later date his previous experience of a capacity to set up micturition at small volumes led him to attempt the manœuvre at low volumes during filling of the bladder, and here the immediate grading of facilitation of waves described in the last section was readily obtained. Moreover, once having obtained such control, Subject A was able to reproduce the phenomenon at will. He had not been able during his first filling to set up such contractions. He felt certain during the second experiment that, as the vesical volume increased, an effort, faintly voluntary to the degree of being almost completely unconscious, was being made continually to hold in check any rising process of voiding. Thus, the absence of any spontaneous disturbance upon attempted micturition during his first filling was referable to a mild inhibition of micturition probably inducing a mild perineal tension. An inability to relax this inhibition sufficiently completely and thus initiate the contraction response was therefore partly a lack of experience of the absence of gravity and the unusual posture, possibly combined with the effect of the distension of the urethra by the catheter. Once the initial unpleasant sensations of passing of the catheter had subsided the subject had no sensation of its presence unless he thought about it for a few seconds, or unless the catheter were moved. The slightest disturbance of the catheter provoked an unpleasant sensation referred to the glans and urethral orifice. It is possible that the absence of fluid entering into the most proximal segment of the urethra had made initiation of contraction at first difficult, but our subsequent observations fail to confirm this view.

It is noteworthy, therefore, and in our opinion of great value in consideration of the shape of the curve of filling pressures of a bladder, that the low type of curve with little or no evidence of spontaneous waves may be solely the result of apprehension and unusual posture upon a normal vesical mechanism. This is undoubtedly the explanation of the reaction of Subject C, who, though suffering no defect whatever in micturition under ordinary circumstances, was quite unable to produce either bladder disturbance or sphincter discharge under the conditions of experiment. Subject B likewise, in his first two experiments, was unable to produce other than small facilitations, and unable to produce sphincter discharge, though able to facilitate contractions in an experiment at a later date.

We conceive that under natural circumstances the process of initiation of micturition resembles much more a series of events such as is seen in Plate I, accompanied by increasing desire for micturition, postponement of the final development of the vesical spasm at will, and not absolutely complete suppression of waves in the intervals.

### (6) THE SENSORY EXPERIENCE OF VESICAL DISTENSION.

Although the sensation of vesical distension in mild degree comes within everyday general experience, and that of more severe distension comes at some time within the notice of most individuals, these sensations are unusually difficult to describe in detail. The disagreeable stinging sensation of catheterization was felt within the penis, more intense towards the meatus, and greatest at the meatus. The passage through the posterior urethra was felt as an exacerbation of this sharp sensation and entry of the catheter within the bladder felt as a lessening of the sharpness of the sensation, which nevertheless persisted for some seconds and then eased gradually.

As the bladder is gradually distended by successive inflows of each 100 c.c. of fluid no sensation whatever is experienced by the subject even with careful introspection, until just before the volume of 300 c.c. is reached (just before 250 c.c. in Subject B). At this time there was faintly discernible on introspection a feeling of the presence of some slight pressure deep in the mid-perineum, likened by Subject A to a very faint pressure from within, and by Subject B to a faint sensation of pressure with movement, "like rivulets running down the urethra." This sensation was not constant, it lasted some few seconds, then disappeared only to return at intervals of some seconds and disappear again. Subject A when experiencing the sensation on a second occasion and then with knowledge of the experience of B, felt that he also could discern movement of the faint pressure and agreed that the sensation was well expressed by the word "rivulets." It was not comparable to any sensation in normal experience. This sensation was not associated with any particular change in the vesical pressure, was not felt with slight waves of pressure occurring just after the volume of 200 c.c. and continued to occur as adaptation was occurring after the volume of 300 c.c. had been reached. As filling proceeded between the volumes of 300 and 400 c.c. at 50 cm. input pressure and narrowed inlet the duration of these periodic sensations increases and the interval lessens. As the sensation developed the factor of movement became more obvious

(" as if some urine were commencing to flow down the urethra "). The vesical pressure remains low, rising slightly as filling proceeds and in both Subjects A and B, just before the volume of 400 is reached, the sensation had become much more definite, but not in any way unpleasant, and could be easily displaced from mind. Subject A described it as the feeling that he could pass urine if he wished to make the attempt. He thought that it was the association of the periodic rivulet sensation with a mild warmth referred vaguely to the distal portion of the penis. It was quite definitely irregularly periodic. Subject B thought the sensation was more continuous, "like a desire to pass water," and decided that he thought the rivulet sensation remained periodic and had more definitely a running fluid quality, while the fresh sensation formed a continuous background not associated with it. He too was able to displace it from mind at will. Both subjects felt that the sensation was a faint desire to micturate which was readily displaced from mind.

In Subject B the next sensation as volume increased was a definite but very slight feeling of abdominal distension which appeared suddenly after a rest for some minutes at a volume of 400 c.c. (Plate III, fig. 8). There is no associated change in vesical pressure, which was 8·7 cm. water at the time. The slight continued sensation of potential micturition and abdominal fullness, with occasional rivulets (now less frequent) remained unaltered until the bladder was subjected to more rapid distension by allowing fluid to run in at 100 cm. pressure and full inlet opening (from 450 c.c. to 500 c.c., and again from 500 c.c. to 600 c.c.). The sensation of fullness increased progressively during these fillings and the " rivulet " sensation again became more definitely running, with some admixture of imminence of micturition (slight " urgency "); the desire for micturition had fully developed. This sensation gradually vanished during the pause at the volume of 500 c.c. (Plate II) and was renewed from the commencement of filling from 500 to 600 c.c. During the later period it occupied the sensorium to such a degree that the subject felt a definite continuous necessity to check the desire. When the volume of 600 c.c. was reached Subject B felt distended, with a slight feeling of flow into the urethra, although there was no evidence that this was occurring. The effort of holding in check the desire for micturition included a movement of extension of the knees. The pressure had risen from 10 cm. of water to 22 cm. of water in sixty seconds. There were no fluctuations of pressure at this time. This sensation remained constant and when the volume later reached 675 c.c. the subject felt a necessity to exert the greatest effort to withhold micturition of which he was capable. Nevertheless when he made an effort to micturate no change occurred. The desire to micturate had gradually merged into a definite pain referred vaguely to the perineum. On emptying the bladder with reservoir level at −30 cm. pressure these sensations passed off in the reverse order of their appearance and abdominal distension had become only very slight at a volume of 450 c.c. The intermittent "rivulet" sensation again became prominent as volumes of 650, 600, 550 and 500 were reached, but no evidence of waves of pressure or of "follow-up" contraction of the bladder appeared.

In Subject A the development of sensation after the first appearance of rivulets followed a similar course. As filling proceeded definite spontaneous waves of pressure made their appearance and at the onset of one of these (reaching 16·2 cm. water), at a volume of about 465 c.c., a sharp increase in the rivulet and warm sensation occurred, not outlasting the wave, and not occurring with other earlier and later smaller waves (13·7 cm. water). With a vesical volume of 500 c.c. Subject A felt that micturition could readily be initiated and a slight abdominal discomfort commenced to be readily perceived. The sudden onset of desire to pass urine, with enhanced urethral flowing sensation, was signalled during a period in which the volume was kept constant at 500 c.c. There is no change whatever in the records of pressure at this time. The sensation was abolished by voluntary postponement, but recurred at intervals of about a minute, then ten seconds (more acutely) and then a strong effort to postpone the desire abolished it successfully until filling had been resumed and a volume of about 545 c.c. reached (slow filling at 50 cm. input pressure). The sensation recurred at decreasing intervals with a more definite feeling of distension of the abdomen as the volume of 600 c.c. was attained (Plate I). With further filling he felt the necessity for continued conscious effort to withhold micturition at a volume of 635 c.c. The onset of the first wave of reactionary contraction of the bladder was associated with a slightly painful and unpleasant sensation referred to the perineum with a slight burning quality. The ultimate development of an undulating violent contraction of the bladder in this subject was associated with a renewal of this sensation in an extremely intense form, and it was then associated with a tingling, prickling sensation felt all over the body. During subsequent emptying Subject A felt relief from all sensation at a volume of 520 c.c.

Subject C experienced no sensation during filling of the bladder until the volume of 175 c.c. was reached, when he complained of a discomfort referred to the penis. With a volume of 200 c.c. he complained of similar discomfort, and again at a volume of 300 c.c. None of these sensations was associated with accompanying change in vesical pressure. On questioning he said he suffered no continued discomfort during filling up to 420 c.c., and subsequent emptying, though he had some sensation of slight distension at 420 c.c. The discomforts complained of were, in our opinion, probably all due to some movement of the patient with consequent movement of the catheter. They were all referred to the meatus. Subject C was an unsatisfactory witness as regards sensations and was evidently much concerned lest the sensations felt during catheterization recurred, and seemed unable to take account of milder sensations.

It is remarkable that a periodic sensation such as the "rivulet" response reported by Subjects A and B was not associated with any periodic change in vesical pressure. Though it was definitely enhanced at certain stages of filling and emptying of the bladder and might thus be thought to be derived from an appreciation of the passage of fluid through the catheter, it was definitely appreciated when no movement of fluid was occurring. We are not inclined to believe that it was derived from the periodic entry of fluid into the posterior urethra, for it occurs at such very low pressures at which, from our subsequent experiments on the sphincters, we are inclined to believe the sphincters both remain closed. Moreover, at these pressures a leak around the catheter of even one drop of fluid was never found to occur. The sensitive manometer should have been capable of detecting any rhythmic entry and regurgitation of fluid within the boundary of the internal sphincter. The "rivulet" sensation, the sensation of abdominal fullness, and the desire to micturate are none of them painful.

The desire to micturate can also appear periodically without accompanying variation in vesical pressure. The afferent stream of information from the bladder must under these circumstances remain constant. We see, therefore, no other alternative than that the abolition of the sensation of desire to pass urine and its subsequent return are processes taking place at a cortical level, and not associated directly with the process of fluctuation in vesical pressure unless that assumes a certain degree. We consider that the fluctuation of the "rivulet" sensation is likewise a cortical fluctuation in the appreciation and interpretation of an extremely mild visceral sensation. We have not experienced this "rivulet" sensation apart from experimental conditions, and therefore are unable to assign to it any definite place in normal vesical sensation.

In a later experiment Subject B remarked the extremely indefinite character of this sensation.

It has been described how, on some occasions, with an unusually sharp wave of vesical pressure the rivulet and running sensation were momentarily enhanced. In the second experiment with Subject A at a time when the outlets were closed, large waves of vesical pressure could be facilitated by will. These reached pressures of well over 100 cm. of water (Plate III, fig. 7). They were each associated during their onset with the rapid development of a sensation of distension deep in the abdomen, a "running" vaguely deep in the perineum and a sharply increasing discomfort referred to the whole perineum. With large contractions the discomfort was felt to be developing into imminent pain so that the subject felt urgently constrained to overcome the process. It is evident, therefore, that the development of a large enough active contraction of the bladder could reproduce the sensations derived from slow passive distension.

The sensation derived from restraint of micturition appears to be solely that due to high tension of the contraction which is suddenly converted from isotonic conditions to isometric.

From the description of vesical sensation served by the hypogastric nerves, from cases where these nerves alone remained in connection with the bladder (Riddoch [22]), it would appear that any or all the sensations described above may reach the spinal cord by these nerves.

## (7) THE VESICAL SPHINCTERS.

Although alteration of the disposition of the catheters to allow closure of one or both sphincters provoked some discomfort to the subject, this discomfort died away in the course of some three to five minutes. In spite of the uneven distension of the posterior urethra and of the presence of the fine ureteric catheter within the internal sphincter no discomfort of any kind was felt apart from some slight scalding as the first jet of fluid passed the sphincter during the first few micturitions. At first this slight scalding caused the subject to exert a momentary interruption in the early course of micturition (Plate V, fig. 9), but he could minimize it after one or two micturitions, and it finally disappeared. No discomfort was felt in the subsequent course of micturition.

With the catheters withdrawn to the disposition shown in fig. 2 C, and the outlet (*h*, fig. 1) of the urethral catheter opened slightly, the record of a complete micturition is shown in Plate IV, figs. 1 and 2. With the signal to relax the perineum there occurs a slight bulging of the perineum and within a short interval the vesical pressure commences to rise, at first slowly and then more steeply, merging into the sharp ascent of a large wave. This rise is most often unaccompanied by any change in the posture of the abdominal wall, or in intrarectal pressure (see especially Plate IV, fig. 2). Early upon the rise of intravesical pressure the sphincter opens at first gradually and then swings steeply to maximal discharge.

Apart from the preliminary jerk of closure which tended to occur in the first micturition the subject made, and associated with a voluntary restraint, the sphincter opening was in general smooth and regular. The undulations which are found in the subsequent course of the urethral pressure reflect, with due allowance for distortion of the actual pressures by the outflow leak, the changes in pressure proceeding in the bladder. Thus after the initial very sharp opening the curve of outflow pressure runs parallel to the change of pressure within the bladder (Plate IV, figs. 1 and 2, and Plate V, fig. 9).

Throughout micturition the bladder remains in powerful contraction. As the termination of the response is approached there occurs a gradual diminution in the vesical pressure. The declining pressure is reflected in a similar decline in the discharge pressure which, however, terminates in an abrupt fall to complete closure. The vesical pressure shows often a further rise as the sphincter closes. This final rise in vesical pressure occurred only when the response secured powerful complete evacuation of a small volume of vesical contents (Plate IV, figs. 1, and 5 K). The remainder of the curve of vesical pressure is then rarely recorded in full, for the pressure usually either rises to extremely high values beyond the range of our recording paper as in Plate IV, fig. 1, or else the openings of the ureteric catheter were occluded by the close enfolding of the vesical wall, as in Plate IV, fig. 2. A more complete record of this "after-contraction" is seen in Plate IV, fig. 3, where a smooth sustained vesical contraction was followed to complete subsidence.

The only constant change which precedes the onset of the rise of vesical pressure with micturition is the relaxation of the perineum. There may be no change in movement of the abdominal wall and no rise in recto-colonic pressure. With the final "after-contraction" of the emptied bladder there is often a rise of intrarectal pressure, and, as in Plate IV, fig. 3, with the termination of a brisk and complete micturition, there is a tendency to suppress respiration and contract the abdominal wall, but this is not either of necessary force or sufficiently constant in appearance to be held responsible for the "after-contraction" wave of vesical pressure.

### *The Commencement of Discharge.*

The pressure at the moment the sphincter opens is not constant and is far below that at which it remains closed during a straining abdominal movement. In the series of consecutive sphincteric discharges observed on one occasion, Plate IV, figs. 4 and 5, the opening pressures were 23 cm., 25 cm., 18 cm., 30 cm., 40 cm., and 43 cm. of water. In such a series of successive responses each of which lessened the volume of the bladder, it is apparent that the vesical pressure at which opening occurs grows greater as the volume grows less. We have not found this inverse relationship between volume and opening pressure applicable in all circumstances, probably owing to the operation of other factors, such as facilitation by speed of filling and variation in the time interval between responses.

When an abdominal movement occurred during the facilitation of a discharge from the sphincter there was always accompanying evidence of perineal relaxation directly preceding concurrent active vesical contraction. On no occasion did the sphincter discharge in response to a passive increase in pressure, even if the catheters were arranged in the disposition shown in fig. 2 B, so that the internal sphincter must alone have been resisting, Plate IV, fig. 7.

In view of the reflex facilitation of micturition in the cat by the presence of fluid in the posterior urethra described by Barrington [4] it was of especial interest to determine the effect of the introduction of fluid into the posterior urethra when the catheters were disposed as in fig. 2 D. The bladder containing 70 c.c. of fluid, a volume at which the subject had previously readily provoked micturition, fluid was introduced into the urethra at a pressure of 100 cm. water. The distension brought no sensation to the subject and was quite ineffective in provoking micturition, even when he made a mild effort to micturate concurrently (Plate V, figs. 5 and 7).

### *Voluntary and Spontaneous Cessation of Discharge.*

A sudden voluntary effort to withhold micturition during its course varies in effect according to the disposition of the catheters. Provided the urethral catheter were sufficiently far withdrawn, the discharge showed an immediate and complete cessation which we believe to be due to the activity of the external sphincter. In this type of immediate voluntary cessation the curve of closure showed an initial small peak of increased pressure before the steep decline to zero (Plate IV, figs. 3 B and 8 E, G). This diphasic type of cessation is always of very brief latency after the signalled commencement of the voluntary effort, and occurs at the commencement of contraction of the perineal floor when that is recorded. If the discharge pressure be still rising when the effort of restraint is made the initial brief increase of pressure is less clear, but some trace of its presence is usually evident as in Plate IV, fig. 5 at G and H and Plate V, fig. 9 F. This type of closure once made can be maintained indefinitely by voluntary effort.

The restraint of vesical contraction when there is no fluid outlet is described in an earlier section. When discharge is occurring, with the onset of closure of the sphincter the vesical pressure often shows a rise to a sharp angle and then declines rapidly at first in a straight line and slowing later to reach resting value if the effort to restrain be continued (Plate IV, fig. 8, Plate V, fig. 9). This sharp angle superimposed upon the curve of vesical relaxation is clearly related to the change of conditions induced by closure of the sphincter, for the vesical wall closing upon diminishing contents abruptly meets the resistance of constant fluid volume. The lack of constancy in its occurrence is probably due to the smallness of outlet usually allowed, so that the bladder was not then diminishing in volume very rapidly. The remainder of decline of the vesical pressure follows the same curve as that following restraint under isometric conditions. The latency of closure of the sphincter is therefore much more brief than that of cessation of vesical contraction.

The preliminary positive wave in the diphasic cessation of discharge would appear to be due to a powerful contraction of the sphincter upon its contents and forceful extrusion of the contents before complete closure of the lumen occurs. The length of urethra embraced by the voluntary muscles of the external sphincter and the abrupt force exerted by its closure, thus endow activity of this sphincter with a characteristic type of termination of discharge. It does not seem to us possible that the M. accelerator urinæ could here participate owing to the presence of the catheter. The relationship of the position of the opening of the catheter to the external sphincter under these circumstances we picture to be that shown diagrammatically in fig. 2 C.

If the catheters be now introduced further, so as to bring the opening of the urethral catheter nearer the bladder, a disposition can be secured where the response to a voluntary effort to restrain micturition becomes modified. The diphasic character of closure is lessened or completely abolished and only with very strong effort is the short latency of complete closure obtained (Plate V, fig. 1). At this level it will be seen that four efforts, each of which is accompanied by powerful contraction of the perineum, succeed in causing abrupt cessation of the outflow, without diphasic swing of the manometer. The fifth effort of restraint in the same micturition, though causing similar subsidence of the rising vesical pressure, secures only a few rapid fluctuations in the pressure of urethral discharge. The outflow continues and its gradual subsidence reflects only the declining vesical pressure which again rises as the effort of restraint is abandoned. The record of perineal movement reveals that the effort has been less powerful than the previous four efforts. There is therefore no sphincter closure. A sixth and slightly more powerful effort secures a complete and immediate closure of the sphincter. A seventh and last effort is less powerful and secures no immediate cessation, while after a delay the outflow shows a small brief interruption, followed by a deeper brief interruption, and after a similar interval a steep complete closure. With this disposition of catheters, therefore, the response to willed effort is modified in a manner which may be interpreted as interference with the full activity of the control of outflow by muscle under voluntary control. The activity of the mechanism which secures the delayed closure featured in the seventh effort of restraint in this record is elucidated by moving the catheters still nearer to the bladder, to a disposition which is shown diagrammatically in fig. 2 B. Here there is reason to believe that the opening of the urethral catheter lies between the internal and external sphincters. Records of the effort of strong voluntary restraint upon the course of micturition now reveal no immediate change in the pressure of discharge (Plate V, fig. 2). The vesical pressure commences to decline after some three to four seconds in response to the restraint, and with it the pressure of discharge. After one or two brief interruptions the discharge ceases abruptly, reaching complete closure in from seven to nine seconds from the onset of the effort, and at a time when the vesical pressure has shown progressive decline. This is further illustrated in Plate V, fig. 3, where, at a larger vesical volume and with more powerful vesical contractions, strong voluntary effort again has no immediate effect on discharge and after a long latency the outflow ceases abruptly. The delay in closure is greater and preliminary irregularity is less the more powerful the accompanying vesical contraction. This type of sphincteric closure is therefore secondary to vesical relaxation. Further introduction of the catheter secures only a continuous record of vesical pressure, with no evidence of sphincteric activity (disposition in fig. 2 A).

It has therefore been found possible to secure a dissociation of the closing mechanism by arranging the catheters at two levels corresponding to control by the voluntary external sphincter on the one hand, and by the involuntary internal sphincter on the other. The existence of an internal sphincter in man has been doubted on anatomical grounds, for it is difficult to dissect a well-defined constricting ring such as is found in lower animals. The formation of a loop from the involuntary muscle of the detrusor covering the anterior wall of the urethral outlet as described by Heiss [14], appears to combine with a semicircle of involuntary muscle applied to the posterior wall of the orifice (sphincter trigonalis of Kalischer) (Wesson [28]), and thus a double loop of involuntary muscle participates in the sphincter. Whatever the actual mechanism of closure of the orifice our records leave us in no doubt that there is a proximal mechanism of constriction which is not immediately under voluntary control, and which serves a reciprocal relationship with vesical contraction. This sphincter is not forced by passive increase of vesical pressure (Plate IV, fig. 7).

### *The Combined Function of the Internal and External Sphincters.*

The immediate closure of the voluntary sphincter in response to voluntary restraint as described above causes a complete cessation of outflow at a time when the internal sphincter must remain patent. Eventual closure of the internal sphincter under these circumstances can be at times registered. If the voluntary effort to restrain be sufficiently brief in duration, and micturition be allowed to proceed within some six seconds (Plate IV, fig. 8, at F and H, fig. 3, following A and B), recommencement of discharge is immediate, and the urethral pressure rises steeply again to a level representing intravesical pressure. Such a record appears to indicate immediate relaxation of the voluntary sphincter and resumption of full discharge, and it would appear unlikely that the internal sphincter had closed at all during the period of restraint. This is also seen after a slightly longer period in the second restraint in Plate V, fig. 4. It will be noted that under these circumstances the onset of the steep opening curve is preceded by a small downward dip, the explanation of which probably lies in the suddenness of relaxation of a tightly closed sphincter. The first restraint in Plate V, fig. 4, shows the effect of a more prolonged effort. A small sharp jerk indicates relaxation of the external sphincter (C, D), and commencing resumption of outflow which ceases jerkily. The discharge recommences in a smooth curve of slow development (E) preceding the development of a fresh vesical contraction. The explanation of this type of reopening involves the assumption that the internal sphincter, secondary to the falling vesical pressure, has been about to close when the external sphincter relaxed. The final downward jerk at D is closure of the internal sphincter, and the smooth S-shaped reopening reflects the opening curve of this sphincter.

The effect of late relaxation of the external sphincter is shown again in Plate IV, fig. 5, where recovery from two long restraints shows a slowly developing urethral pressure on resumption of micturition, at E and H, revealing the gradual relaxation of the internal sphincter.

The internal sphincter therefore closes after a delay, not only when it alone controls the discharge from the bladder, but also when the external sphincter has already closed. The reciprocal relationship with vesical pressure is maintained.

With the catheters arranged in the disposition shown in fig. 2 D, it was found that, with a vesical volume of 70 c.c. and the subject not restraining, fluid introduced into the posterior urethra did not affect the pressure from the other catheter opening distal to the external sphincter, which therefore must remain closed under these conditions (Plate V, fig. 5), even when under these circumstances the subject relaxes the perineum in attempting to commence micturition, and even when an abdominal strain is added (Plate V, fig. 7). Under these circumstances fluid introduced into the posterior urethra under moderate pressure enters the bladder but does not pass out through the external sphincter which remains closed. The subsequent record of some vesical contraction in Plate V, fig. 7, reveals the eventual occurrence of vesical contraction in response to the continued effort to micturate with a filled bladder, but the urethral pressure does not rise until the vesical pressure is rising steadily and full micturition might be expected under any circumstances. With the same disposition of catheters in another experiment, the pressure chambers of both catheters being arranged to have a leak, the bladder having previously been filled, a micturition was allowed and the effects of the two sphincters recorded (Plate V, fig. 6). Here it will be seen that the internal sphincter opens earlier than the external sphincter, and in a more gradual manner (the narrow lumen of the ureteric catheter though not affecting latency in any recognizable degree at this speed of record may nevertheless distort the actual curve of onset so that a sharp angle may be blunted). An effort of voluntary restraint closes the external sphincter in characteristic manner while the internal sphincter pressure declines slowly (Plate V, fig. 6 C). With cessation of voluntary restraint the external sphincter reopens at E, only to close again at F, as the internal sphincter is about to close gradually. The discharge is renewed and allowed to run its course to spontaneous cessation and again the external sphincter closes abruptly at I, leaving the internal sphincter still patent but about to close in a more gradual manner. An abdominal strain immediately after this (at K in the same figure) fails to disturb the pressure in the ureteric catheter and thus demonstrates that the internal sphincter has closed completely.

The external sphincter, therefore, not only closes first at natural termination of a micturition but also remains closed even when an effort is made to micturate and the perineum is relaxed. It is only when vesical contraction has commenced and has reached a degree sufficient to be accompanied by opening of the internal sphincter that relaxation of the tone of the external sphincter, sufficient to allow the passage of fluid, occurs.

## (8) The Reactions of the Rectum in Relation to Vesical Function.

A full analysis of rectal behaviour has not been attempted, but some points of interest emerge in our records. The passage of a balloon into the rectum produced a contraction of the rectal sphincter which was easily overcome. As the balloon gained entrance into the anal canal a sharp discomfort referred to the anus, associated with a desire to expel the foreign body, was experienced. When the balloon was introduced 7 to 10 cm. and then allowed to remain still, these sensations, over a period varying from five to ten minutes, gradually subsided and the subject was aware of a sensation referred to the anus only upon introspection. The feeling of defæcation was renewed by further movement of the balloon and distension of the latter caused a sharp return of the discomfort. During the experiment the balloon tended to move inwards so that its tip was as much as 19 cm. from the anus.

The record of rectal pressure shows variations in abdominal pressure, including those caused by respiration, and changes in rectal pressure induced by contraction or relaxation of the bowel wall. During abdominal straining movements the rectal tracing mirrors the vesical record (Plate II, F, G, H, I, and Plate IV, fig. 6). Rapid filling of the bladder induced a slight rise of intrarectal pressure when the volume of fluid in the bladder was high. In Subject A the rectal pressure rose 8 cm. of water during filling to 600 c.c. In Subject B at the end of a prolonged filling to 725 c.c. the rectal pressure rose 3 cm. During a spontaneous wave of contraction of the bladder there is no constant change in rectal pressure. In the absence of a change of intra-abdominal pressure the rectal pressure remains constant. Perineal movement alone has but little effect upon the rectal pressure, a determined perineal contraction when the bladder contained 130 c.c. produced an inconstant slight rise in rectal pressure, probably explained by a concurrent increase in abdominal pressure.

Subjects B and C displayed no other variations in rectal pressure. During the series of discharges of the sphincters obtained in Subject A slight rises of rectal pressure without corresponding abdominal movement occurred with each vesical contraction. Such rises are seen in Plate IV, fig. 8. In one response this increase became much more definite and eighty-five seconds later, when the vesical disturbance had completely subsided, a series of three isolated rectal contractions occurred at intervals of approximately thirty-five seconds with no other concommitant phenomenon. Straining movements set up no such contractions. A large rectal contraction which raised the intrarectal tension by 32 cm. of water occurred during a period of filling of the bladder. At the same time the subject recorded "a feeling of rectal contraction, a desire to evacuate the rectum." Two such contractions, each accompanied by the same sensation, are recorded in Plate V, fig. 8. Sphincteric responses obtained later were not associated with a change in rectal pressure, but at the termination of the vesical contraction a mild spontaneous increase in rectal pressure sometimes occurred (Plate V, fig. 9 H), and this is here well contrasted with the effect of an abdominal strain which precedes the sphincteric discharge.

In a subsequent experiment the distance from the tip of the rectal balloon to the anus was 11 cm. instead of 19 cm. as in the above experiment. On this occasion no rhythmical contractions of the rectum were observed, but when full uninhibited vesical discharges of small volumes were being recorded (Plate IV, figs. 1, 2 and 3) a rectal contraction occurred as the bladder was contracting strongly after it had expelled its contents. In the third response, at the termination of complete expulsion, the intravesical pressure mounted to a higher level, and coincidently a sharp rise in rectal pressure of 32 cm. of water occurred and rapidly subsided. It is of interest to note that a perineal contraction occurs synchronously and mirrors the rectal record. It may be concluded that the rectum or distal pelvic colon shows spontaneous contractions which vesical activity tends to stimulate.

## (9) Discussion.

An outstanding problem in the physiology of micturition, and the key to full understanding of nervous disturbances of that function, is the determination of the means by which the bladder and sphincters, which possess a definite measure of autonomy, are subjugated to the control of will. The most direct approach to the question appears to be an analysis of isometric records of contraction of the vesical musculature. The degree of willed control of such contractions is not only dependent upon the degree of distension of the bladder, but also upon the amount of excitability remaining from previous events. Rapid increase in volume facilitates the effect of willed effort to micturate. Preceding suppression of a vesical contraction appears for a short period to give especial ease in the voluntary production of other contractions. A certain volume of contents is necessary before any evidence of voluntary effect can be obtained. In one experiment in Subject A, no evidence of voluntary effect was obtained with volumes below 600 c.c., on one occasion below 125 c.c., and another occasion 50 c.c. We may make a provisional assumption that an unconscious, and presumably spinal, vesical mechanism requires the stimulation of distension before voluntary control becomes possible: The varying degree of distension necessary at different times in the same subject, lessening in each successive experiment, suggests that the variability of threshold is related more to the fluctuations of psychological factors than to variation in the spinal vesical reflexes.

Extraneous and apparently unrelated factors such as unusual posture or embarrassing circumstances can completely negative willed control. The failure of Subject C to provoke any vesical disturbance by effort of will was complete at the volumes used. In no experiment was ability to open the sphincters present when no vesical contraction could be evoked. Failure of voluntary control implied failure both of vesical control and sphincter control. Unwilled, but nevertheless estimable, factors of a psychological order appears therefore to affect the function of micturition as a whole.

Micturition, to a greater degree than any other voluntary function, has a functional as opposed to an anatomical conception in the cerebral cortex. All will is directed to the complete act. Indeed Genouville [10] has maintained that willed micturition is not comparable to voluntary movement at all, for it entails thought of the completed process, just as willed effort to salivate requires an indirect process. The question is discussed at length by Adler [1]. It does not appear possible for voluntary effort to be directed to either the bladder or the sphincter alone. An introspective analysis of micturition reveals a concept of a series of sensations each of which is extremely vague in definition, with the exception of a contraction of the abdominal wall. This latter we have shown, in full agreement with Mosso and Pellacani [18], to be unnecessary for the induction of micturition. The next most definite and constant perceptual event in the voluntary initiation of micturition is a relaxation of the perineum. The constancy of its relationship to the onset of micturition is demonstrated by records. Micturition or vesical contraction never occurred without movement of the perineum. The latency between the onset of perineal relaxation and the onset of vesical contraction varies within wide limits. When the latency is long as in Plate III, fig. 1, and Plate II, at V, there does not appear any possibility that the actual active movement of relaxation has any direct, immediate effect. We have found no evidence that the entry of fluid into the posterior urethra plays any part in initiating micturition or in vesical contraction. The only factor of importance arising from perineal relaxation, therefore, would appear to be the continuance of a relaxed posture of the muscles. This movement of the voluntary muscles which surround the urethra appears to support Müller's [19] theory that there is reflected from them an afferent stimulus which exerts a reflex effect in evoking vesical contraction. The conception was furthered by the description of mild reflex stimulation of vesical contraction by distension of this portion of the urethra in animals by Barrington [4]. The effect of distension by fluid was in our experiments negative, but the possibility of a proprioceptive afferent stimulus for the reflex arising from the muscles themselves is difficult to exclude. We would stress, however, that perineal relaxation is not always effective in provoking vesical contraction and occurs in circumstances, such as straining at stool, when micturition is in abeyance. The movement of the perineum may be considered provisionally as an "associated movement"—resembling the movement of the ears when moving the eyes to one or other side, or movement of the arms in yawning.

The degree of voluntary control of vesical contraction, once psychological factors are negatived and the volume of contents brought to a moderate value, is most striking. The observed latencies in these experiments may be very short indeed and give an impression of a degree of control much more complete for excitation of vesical contraction than was suggested by the work of Mosso and Pellacani [18]. Comparison of various degrees of vesical contractions produced by willed effort shows every stage from simple enhancement of involuntary rhythmic fluctuations, more or less complete fusion of such small waves, to smooth powerful high-tension contractions. Graded voluntary suppression of vesical activity reveals the reverse decomposition. It would seem, therefore, that voluntary control is expressed by the facilitation or inhibition of a local contractile mechanism related to co-ordinating neurones of the antero-lateral horns of the lumbosacral cord.

These "voluntary contractions" of the bladder present, therefore, two peculiarities by which they differ radically from all other voluntary movement. They require conditions which evoke spontaneous activity of the local mechanism, and even when these are fulfilled they can be completely in abeyance despite the most earnest effort of will. Furthermore, they reveal even in their most developed form the rhythmical character of the simple involuntary response of the organ. Though varying grades of intention to micturate could facilitate varying degrees of response, it was also found that the subject had only a vague notion of the degree of effect he was about to produce in any given attempt. Control of magnitude of response inevitably involved the employment of some admixture of restraint, and as far as introspection could determine was composed of a voluntary effort to micturate, itself but little variable, mingled with varying magnitude of restraint.

In marked contrast to the facilitation of vesical contraction lies the manner of its suppression. Apart from the ultimate reaction of the most extreme distension, a full-willed effort of restraint of micturition could, after a brief latency, secure complete abolition of vesical contraction. Voluntary suppression of vesical activity is absolute and unequivocal. The latency is such as may reasonably be supposed to represent the intrinsic slowness of smooth muscle in reaching the decline of its twitch contraction. Restraint of micturition can further be graduated in infinite degree. It therefore appears certain that voluntary innervation can inhibit neurones correlating the activity of the contractile units of the wall of the bladder. Goltz [11] first showed that destruction of the lumbosacral portion of the spinal cord in animals was followed by complete abolition of vesical function. There is some evidence, therefore, that the nervous mechanism related to co-ordinated spontaneous vesical contraction includes neurones within the spinal cord. The site of voluntary inhibtion may therefore be related to the sacral segments, and the insignificant inhibitory effect on the bladder resulting from stimulation of the nerve supply suggests that such is the case. The absence of power of voluntary restraint in men with sacral lesions described by Head and Riddoch [13] reveals no willed inhibitory function in the hypogastric innervation. The spontaneous activity which occurs in such cases moreover appears more directly related to the vesical plexus.

The conditions attached to the performance of voluntary facilitation of vesical contraction open considerable doubt as to the existence of any direct voluntary excitation of vesical contraction. It is profitable to consider whether the whole control of vesical contraction by will may be by means of varying inhibition of the natural contractile reaction of the local vesical mechanism. Thus the powerful contractions with brief latency which we have described can be interpreted as sudden rebound of the local vesical autonomic contractile mechanism following the onset of removal of a damping, inhibitory influence from higher nervous centres. Effort to micturate is on this view an effort to disperse an inhibitory suppression of micturition, consciously or unconsciously applied. It may be argued that the period of inactivity would on this view require conscious effort of control and the act of commencement of micturition would more obviously necessitate a release from control. The type of vesical contraction produced immediately following upon rapid distension of the organ is undoubtedly of this order. The subject allows a release from a restraint of which he is definitely conscious. We would urge that in the induction of all voluntary micturition there exists no immediate necessity for the postulation of a direct excitatory pathway.

The development of voluntary control of micturition in the infant strongly suggests that inhibition of micturition is not only the main function exercised by will in this connection but may be the *only* function. That the mechanism should develop a capacity to function without intrusion upon consciousness, and to emerge into and be banished from consciousness at will, may be readily likened to the same property possessed by the function of walking or running.

Our records of filling of the bladder reveal rhythmical fluctuation of vesical pressure occurring from time to time as filling proceeds, and also at intervals with constant volume. These fluctuations in the vesical contractile mechanism intrude upon consciousness only when they reach a certain degree of magnitude. Their suppression at higher volumes becomes a conscious act, but at lower volumes and when not provoked by distension they disappear without any intrusion upon consciousness or variation in local conditions. If they are evidence of stimulation of the local contractile mechanism alone they should continue to occur in continuous series of increasing tempo. Their occurrence may therefore be regarded as variations in degree of involuntary suppression and further evidence of readjustment at an unconscious level.

These observations upon the modification of the automatic, probably reflex, activity of the bladder by willed efforts, have in our view a profound influence upon the interpretation of the volume-pressure curve as measured by the Rose cystometer, and used to estimate disturbances of vesical innervation [23]. The low flat curve pictured in fig. 3 B, *b*, is the curve of the distension of an organ so well subjected to higher nervous depression, that its behaviour appears identical with that of a paralysed bladder. Variation in degree of voluntary control can produce a higher curve, rising to irregular peaks if free contractions are allowed. The discomfort of powerful contraction appears to be of considerable importance in determining the flatness of the normal filling curve, and the interpretation of irregular variations of this curve requires consideration of the possibility of facilitations and restraints exercised by the subject.

When the analysis of micturition is further extended to include the function of the sphincters it becomes at once apparent that the one very definite factor of voluntary control of vesical activity, namely inhibition, has a direct counterpart in the sphincteric mechanism. Voluntary restraint of micturition occasions both inevitable cessation of vesical activity and immediate powerful, direct closure of a distal part of the sphincter. The obvious voluntary control of this sphincteric mechanism identifies it with the M. compressor urethrae, or external sphincter of Henle. Its activity in response to voluntary effort is documented in our records by a diphasic excursion of very brief latency, with an associated contraction of other voluntary muscles of the perineum.

The activity of the external sphincter in the course of voluntary initiation of micturition and its spontaneous cessation is of a different kind. Despite relaxation of other voluntary muscles of the perineum in the course of the effort to micturate, the sphincter does not appear to relax until after the internal sphincter has relaxed sufficiently to allow fluid to enter the posterior urethra. Distension of the posterior urethra by fluid does not secure relaxation of the external sphincter even when combined with voluntary effort to micturate. The external sphincter appears, therefore, to maintain a tonic contraction subject only to relaxation of the internal sphincter or contraction of the bladder. Young [29] maintains that the external sphincter remains closed if the internal sphincter is dilated by an instrument especially adapted to the purpose. Direct relaxation of the internal sphincter therefore appears to be the only factor determining relaxation of the external sphincter.

Our experiments have confirmed the work of Rehfisch [21] which revealed the continuous function of a closing mechanism proximal to that which is subject to direct voluntary control, and we would identify this with the internal sphincter of Henle at the neck of the bladder. We have found that this sphincter not only opens on effort to micturate, but also can close following effort of restraint. Such closing and opening may continue until the bladder is emptied.

The internal sphincter cannot be induced to open without the presence of vesical contraction, and we consider this finding to be one of considerable importance to the full understanding of the process of micturition. Passive increase of intravesical pressure does not alone suffice to render the sphincter patent, however great the volume embraced by the bladder. Not only is the relaxation of this sphincter related constantly to the accrescence of vesical pressure, but its closure is a process inseparable from the occurrence of vesical relaxation. The function of the sphincter is reciprocal with that of the vesical wall. The opening of the sphincter occurs earlier on the rising wave of vesical contraction, and its spontaneous closure earlier upon the decline of the wave, the greater the volume of fluid in the bladder, but no other effect of variation in volume was observed. Closure of the internal sphincter is directly related to subsidence of vesical contraction, and the characteristic delay in the response of this sphincter to willed restraint is the outcome of this relationship.

Voluntary inhibition of vesical contraction brings about an indirect closure of the internal sphincter. There is some evidence that the sphincter contracts in a series of rhythmical jerks as if it possessed an inherent contractile rhythm several times more rapid than that of the smooth muscle of the bladder. There is no evidence that it reacts in a manner other than the direct inverse of that of the detrusor muscle of the vesical wall. Though there may be minor lessening of contraction of the sphincter accompanying minor contraction waves in the bladder (Schwarz [24]), our method allows only the registration of the moment the lumen becomes patent so that it is not unlikely that the sphincter contraction may reflect the direct opposite of the vesical contraction without any especial arrangement to adjust the occasion of its opening.

The work of Wesson [28] and the illuminating suggestion of Young and Macht [30], that a slip of the muscle of the trigone actively dilates the internal sphincter, provides a means whereby contraction of the vesical trigone actively tends to open the internal sphincter. Our method of experiment does not allow a direct opinion upon the question, but the evidence from physiological experiment upon the internal sphincter of animals such as the cat provides ample evidence of the existence of a direct reciprocal innervation of detrusor and internal sphincter. The reciprocation between the bladder and external sphincter has probably a reflex basis, the fifth reflex of Barrington [4].

The final event in micturition, if the bladder reach complete evacuation, consists of a complex abdominal, vesical and rectal contraction, associated with slow closure of the internal sphincter and a sudden closure of the external sphincter. The external sphincter appears to close first.

Normal sensation from the bladder is derived in part from the tension to which the vesical contents is subjected. Mosso and Pellacani [18] and Genouville [10] would relate all sensation directly to the intensity of vesical pressure, while Guyon [12] showed the fluctuation of sensation with waves of contraction of the bladder. When the volume is progressively increased there is evoked a series of sensations with the vague reference which characterizes all visceral feeling, and culminating in actual pain. These sensations are not in our experiments directly related to the pressure of the vesical contents, for powerful passive pressure upon the bladder when the volume is low gives rise to no such sensations as occur when the volume is increased, though the pressure may then still remain quite low. We have not found a pressure of 18 cm. of water necessary to evoke desire for micturition, indeed discomfort may be extreme at much lower pressures. Sensation is not necessarily evoked by a spontaneous vesical contraction, though if the volume is such as to evoke some sensation such a contraction determines an immediate increase of it. If the active vesical contraction be sufficiently powerful the whole series of sensations to acutepain may be experienced as the contraction gains tension, though the volume remain so small that the resting bladder gives no sensation at all. The sensory end-organs concerned therefore have an adequate stimulus both in passive increase in length of muscle fibre and active increase in tension, and by some means these can sum their stimulation in infinite series. The resultant sensation, if moderately constant, can by some process be suppressed from consciousness. We have found no evidence to support the contention first brought forward by Goltz [11] that desire for micturition is produced by the entry of fluid into the posterior urethra. Fluctuations in its perception do not necessarily reflect equivalent fluctuations in either degree of distension or active contraction, and this type of variation in sensation presumably possesses a psychological basis.

The process of storage of urine and its evacuation occurs, therefore, in a reservoir of which the distension excites a tendency to an automatic discharge. The primary factor in discharge is contraction of the wall of the bladder with an accompanying secondary reciprocal relaxation of both sphincters. The control of discharge and the utilization of the reservoir for volumes above about 50 c.c. depend upon unconscious and conscious inhibition of vesical contraction. If necessary this may be reinforced by active voluntary excitation of the external sphincter until the vesical contraction is overcome. More usually the process pursues a course of progressive complete adaptation without the occurrence of sufficiently powerful vesical contractions to be accompanied by full relaxation of the internal sphincter until conscious and unconscious control of vesical contraction is released by a voluntary effort.

## (10) SUMMARY OF CONCLUSIONS.

(1) A method is described by which records of the pressure within the normal urinary bladder may be obtained during manipulations of the volume of the organ and during micturition. By this method it is shown that the human bladder reacts to distension by contraction of its wall.

(2) The reactionary contraction which is evoked by distension of the bladder is controlled by a restraining effect which at low volumes is subconscious in operation. This process of adaptation, or modification of reaction, intrudes upon consciousness in greater degree as volume increases.

(3) The normal sensations perceived are set up by the process of adaptation only when the active vesical contractions concerned reach a threshold intensity. Otherwise sensation is derived from passive enlargement of the organ. Sensation is thus only indirectly related to pressure, and in such a way that increase in area of vesical wall (increase of length of muscle fibre), within limits of only very slight corresponding increase of passive internal pressure, markedly lower the threshold at which added spontaneous active contractions can produce sensation.

(4) Apart from a faint background of maintained tonic activity,

spontaneous vesical activity takes the form of waves of contraction appearing in rhythmical progressions.

(5) Willed effort to micturate can evoke powerful contractions of the bladder with very brief latency of development. These contractions in their form and rhythm differ in no way from the spontaneous reaction of the viscus.

(6) Relaxation of the musculature of the perineum appears to be inseparably associated with the voluntary development of micturition. It is not regarded as an essential factor of the process but as a closely linked "associated movement." It is not accompanied by relaxation of the external (voluntary) sphincter. Contraction of the abdominal wall is a less closely associated movement which can be dissociated from micturition completely. A tendency to spontaneous activity of the rectum and lower pelvic colon is a much less common association with micturition.

(7) Voluntary restraint of micturition has a direct effect on the contraction of the bladder, so that the spontaneous nervous discharges responsible for vesical contractions can be completely inhibited with ease. It is suggested that the site of impact of this inhibition is on outgoing neurones of the spinal cord. Contraction of the perineal musculature is closely associated with voluntary restraint as is also direct and immediate closure of the external sphincter.

(8) The internal (involuntary) sphincter contracts and relaxes in reciprocal relationship with the detrusor muscle of the wall of the bladder. It is not under voluntary control, and its reaction to voluntary effort to control micturition is entirely secondary to the effect on detrusor activity. The closure of this sphincter is definite, and is continuously maintained during intervals of slight or absent vesical contraction.

(9) The external (voluntary) sphincter is also maintained in closed posture and opens only after opening of the internal sphincter. It closes spontaneously at the termination of micturition before the internal sphincter has closed. Closure in response to effort of will is more powerful. It appears not to be relaxed by voluntary effort.

(10) Normal micturition is entirely secondary to active contraction of the bladder. From the direct nature of the effort of voluntary restraint and the indirect nature of voluntary facilitation, voluntary control of micturition is regarded as being effected solely by variation in voluntary and subconscious inhibition of the mechanism of spontaneous reaction to distension.

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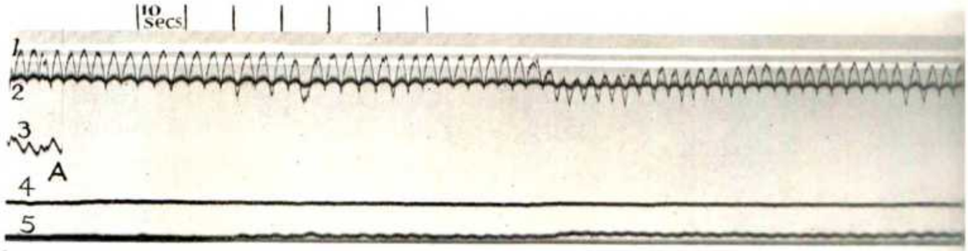
## PLATE I.

Showing variation of vesical pressure during periodic filling of the bladder to a volume of 725 c.c., and the eventual reactions. All records read from left to right. Fine vertical lines in continuous series at top of record mark ⅕ sec. For a minute each tenth second is stressed by a vertical black line. The speed is constant throughout. Two parallel white lines at the top record volume and events. The moving lines of the record are numbered: 1, the fluctuations in pressure of a balloon at the umbilicus; downward movement corresponds to outward movement of the abdominal wall. 2, the pressure in a balloon introduced into the rectum; downward movement for increase in pressure. 3, the pressure in the pressure chamber of the urethral catheter (i.e., within *c* in text fig. 1). Upward movement for increase of pressure. 4, intravesical pressure transmitted from pressure chamber connected to small catheter (text fig. 1 *e*). The calibration of the pressures recorded by this manometer is shown in a scale in centimetres of water with zero corresponding to level of symphysis pubis.

At A, bladder empty, fluid input tap opened, reservoir level at 50 cm. water input pressure. At notch in upper signal, 50 c.c. has run in. Three waves of increasing vesical pressure occur at B, C, and D. Input closed when 100 c.c. had entered bladder (during D). At E an accidental contact with glans causes involuntary wince. Inflow again commenced at G; slow waves of pressure occur as volume rises to 200 c.c., and further waves during filling 200 to 300 c.c. (I to K.) At J a faint sensation of pressure developed in deep urethra. Intermittent return of this sensation during filling to 300 to 400 c.c. (L to M.) Subsequent small waves are more evident during filling to 500 c.c. (N to Q.) Rest period of 256 sec. (Q to R) is uneventful and abbreviated. During filling to 600 c.c. (R to V) no waves occur, but at S a sensation of abdominal fullness, more definite at signals T and U. Increasing sensation of fullness and urethral discomfort during the rest period of 290 sec. at 600 c.c. At W filling resumed, subject "definitely holding" at X, and at Y, sharp discomfort referred to perineum; 16 sec. later urgent desire to micturate and sharp discomfort, associated with spontaneous wave of 18 cm. pressure. Sixteen seconds later another wave *(a)* with similar sensation. Discomfort increased steadily without further waves to volume 725 c.c. *(c)*. Discomfort now accompanied by tingling all over body, more intense with contractions *(d)*; a powerful effort to restrain abolished the greater part of the sensations and the contraction subsided, to return at *(e)* and *(f)*. In spite of effort to restrain, pressure fluctuated at a high level and subject implored relief. Outflow opened at 0 cm. pressure at *(g)*. Now for first time fluid began to escape around the catheter. Discomfort again intense at *(i)* 125 c.c. forced out by wave *(j)*, with renewal of discomfort and pressure. At *(k)* a further 50 c.c. evacuated. Both catheters extruded from bladder at *(l)*.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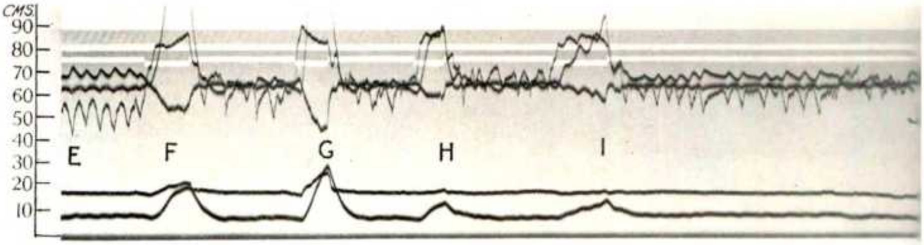
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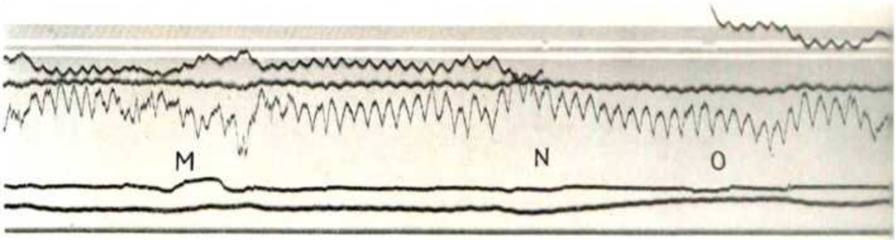
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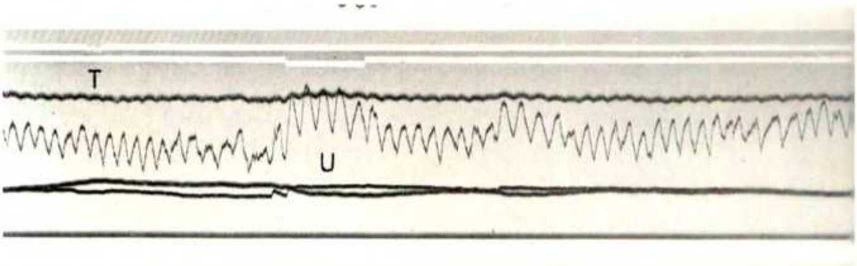
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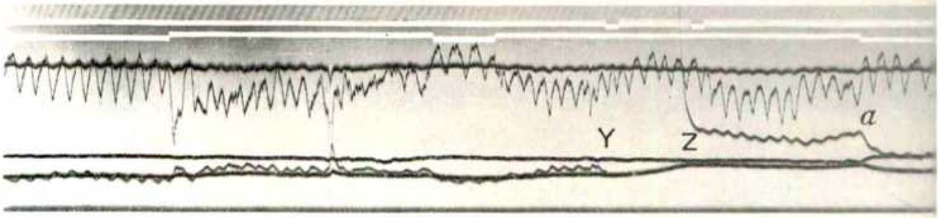
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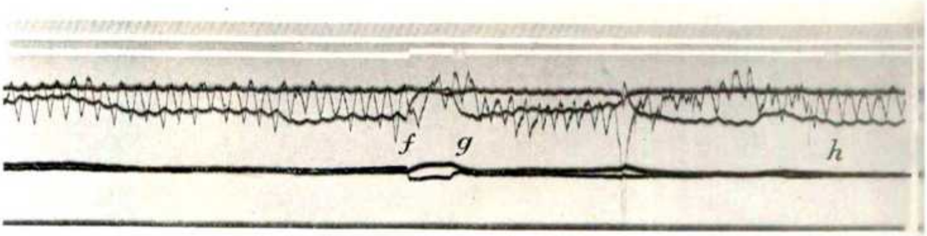
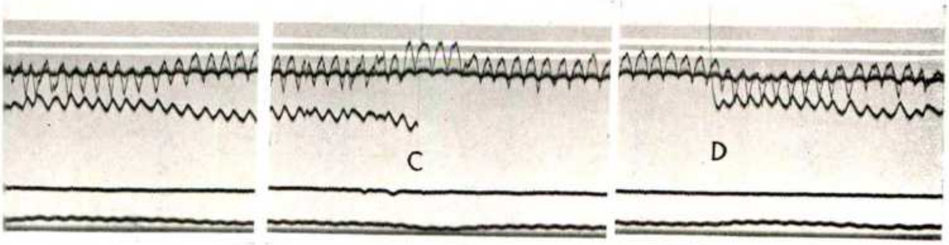

f
g
h

# PLATE II.

Showing events during filling to volume of 675 c.c. and attempts to evoke a vesical contraction, in the course of the first experiment on subject B. Time and signals recorded as in Plate I. The moving lines are: 1, abdominal movement; 2, intra-rectal pressure (downward excursion for increase in pressure as in Plate I); 3, urethral pressure, or reservoir pressure if input open; 4, record of pressure in balloon on the perineum, upward movement shows outward movement of perineum; 5, intra-vesical pressure from ureteric catheter, calibrated on scale in centimetres water above level of symphysis pubis. Catheters as in disposition of text fig. 2 A. Bladder empty.

At A, inflow commenced, reservoir pressure 50 cm.; gradual increase of vesical pressure. After filling for three minutes volume reached 100 c.c., and pressure in bladder 2·8 cm. Inflow closed (B); slight adaptation occurred at constant volume. Filling resumed to 200 c.c. (C-D). Uneventful record of filling to 400 c.c. excluded from Plate. Pressure now 5 cm. and "rivulet" sensation had commenced (see text). Onset of sensation of distension, shown as fig. 8, Plate III. Then the subject made four "straining" movements of the abdomen and diaphragm (F, G, H, and I). 50 c.c. allowed to run in at 100 cm. pressure (J to K). At L an attempt to relax as if about to micturate. At M another attempt with especial effort to relax perineum. A further 50 c.c. at 100 cm. pressure run in from N to O. A strain of diaphragm and abdominal wall at P. Two doubtful spontaneous waves of vesical pressure, at Q and R, associated with rise of abdominal pressure. Filling from 500 to 600 c.c. at 100 cm. pressure (S-T), with immediate increase of abdominal discomfort. An attempt to relax perineum and micturate (U) caused a slight fall of vesical pressure. Urgent desire to micturate and sensation of distension of abdomen continued; knees extended in attempt to ease discomfort. Prolonged effort to micturate commenced at V, resulting in a sensation of commencing micturition and a rise of vesical pressure, which falls in response to a strong effort to restrain, commenced at W. No escape of fluid around catheter. Relaxation of effort to restrain at X; 25 c.c. introduced at 100 cm. pressure, Y to Z. Further effort to micturate (*a*), culminating in strain (*b*), without independent effect on vesical pressure. Filling to 675 c.c. (*c* to *d*); pressure now 32 cm. water. Subject felt necessity to restrain as much as possible, with acute discomfort, but attempt to micturate (*e-f*) ineffective. "Cold shivers" signalled at (*g*) and (*h*). Reservoir lowered to minus 30 cm. and fluid run out (*i*); outflow closed at 600 c.c. (*j*), with no evidence of spontaneous rise of pressure within bladder (*j* to *k*). No evidence of "follow-up" contraction of bladder as it was subsequently emptied to 400 c.c. (not shown).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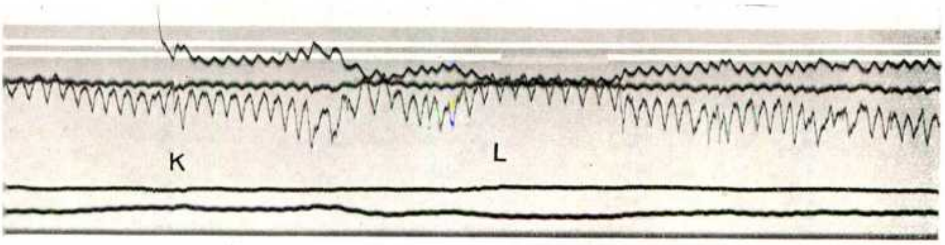
D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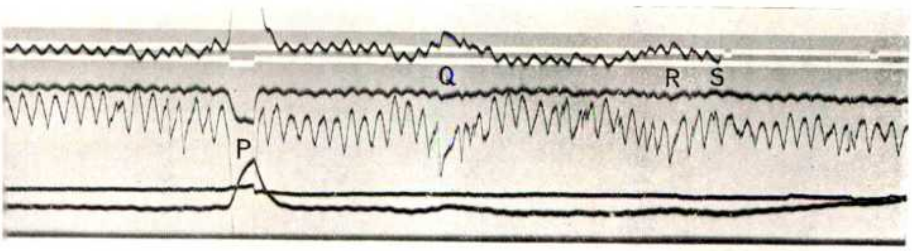
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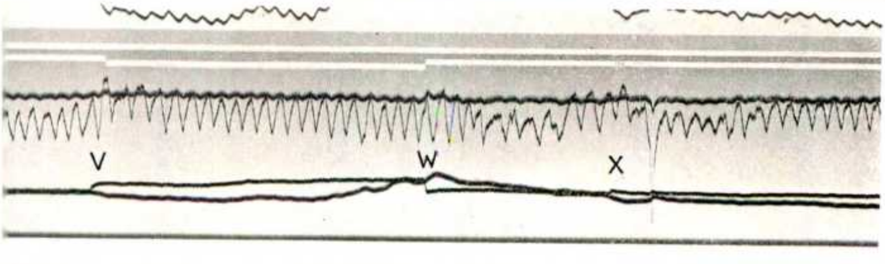
R
S
P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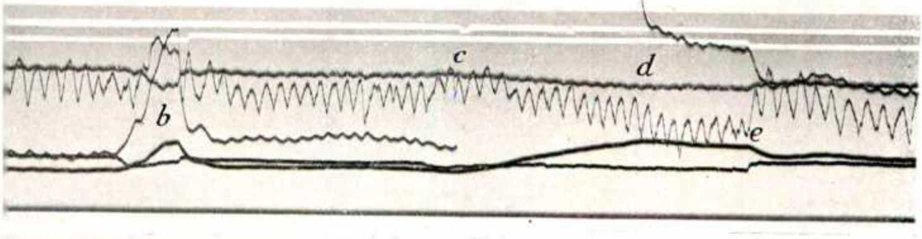
W
X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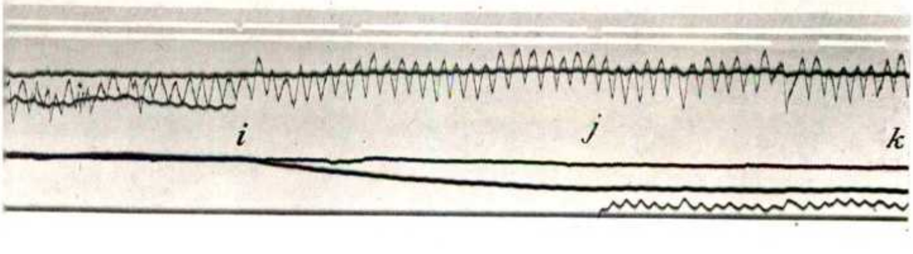

i
j
k

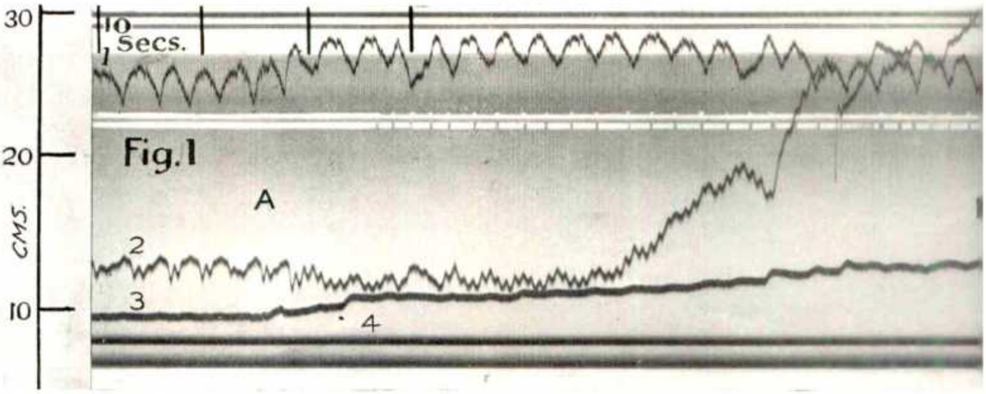


Fig.1

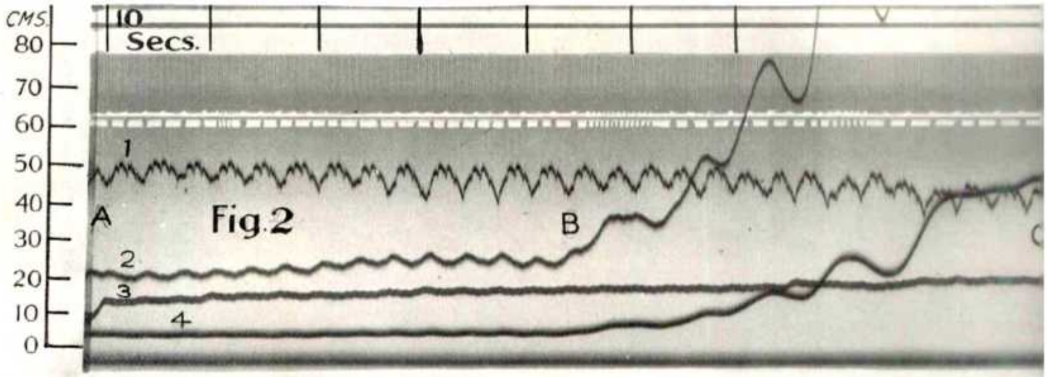


Fig.2

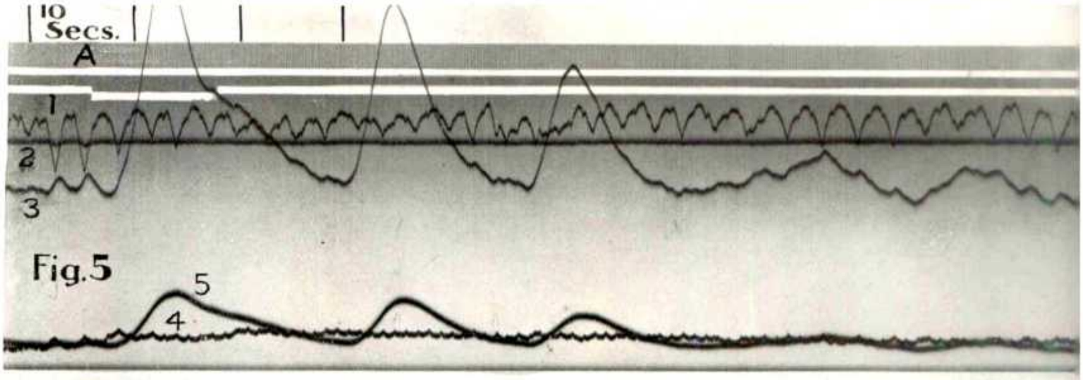


Fig.5

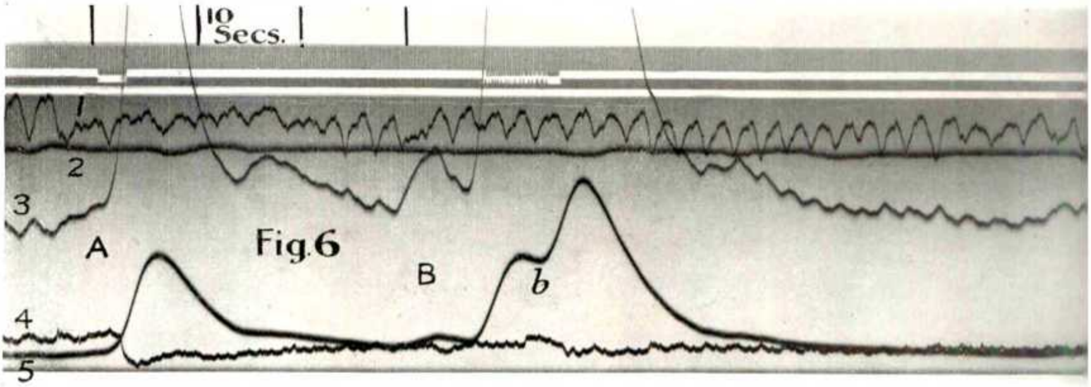


Fig.6

I.

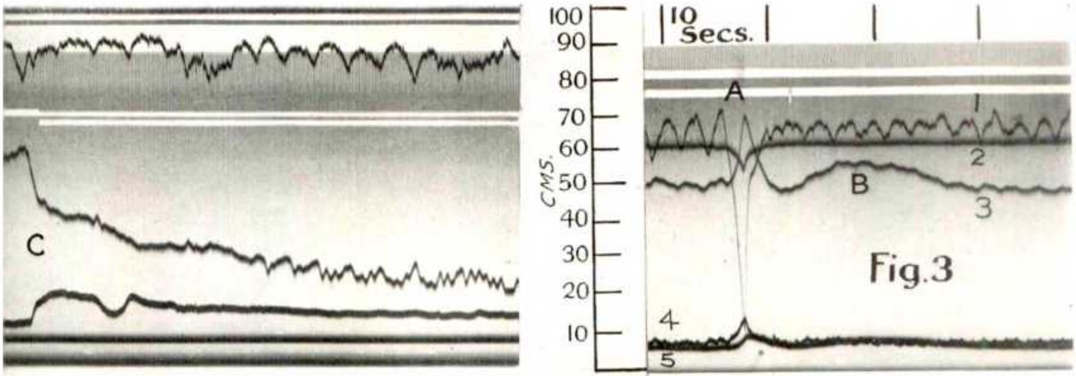


Fig. 3

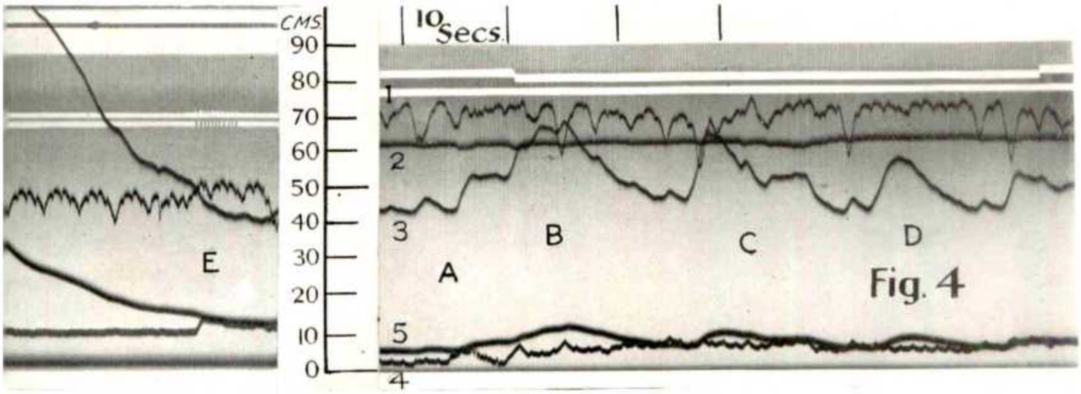


Fig. 4

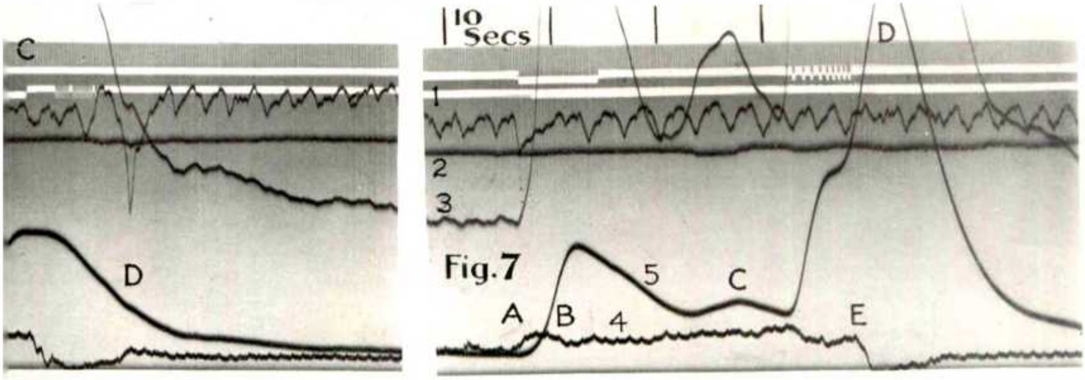


Fig. 7

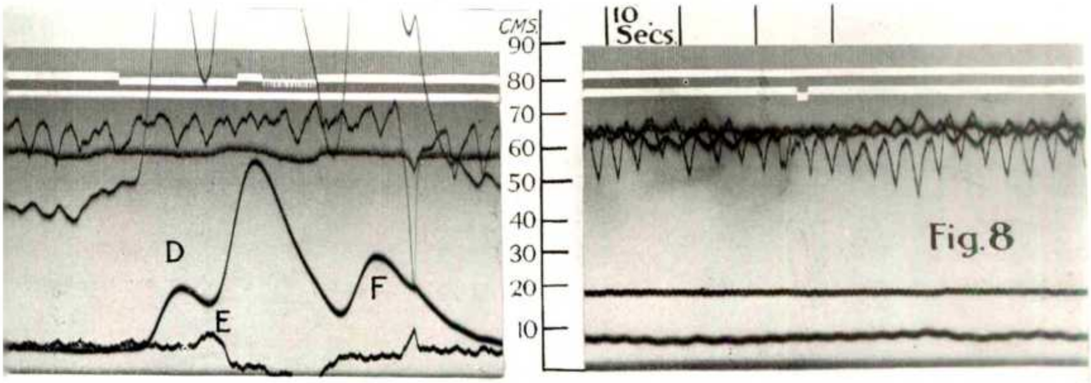


Fig. 8

## PLATE III.

Figures illustrating contraction of the bladder in response to willed effort under isometric (constant volume) conditions.

FIG. 1.—The moving lines on the record are: 1, abdominal movement; 2, intravesical pressure indicated by a sensitive manometer (urethral catheter); 3, perineal movement. Volume of vesical contents, 927 c.c. Subject B, third experiment. Commencement of attempt to micturate at A, continued to B; the vesical pressure responded. A strong effort to restrain micturition was commenced at B. Cessation of effort to restrain at C.

FIG. 2.—Later attempt with smaller volume. Records 1, 2 and 3 as in fig. 1; tracing 4 shows vesical pressure through ureteric catheter calibrated on scale. Volume, 200 c.c. Commencement of effort to micturate at A. Vesical contraction at B and C; effort to restrain at D to E.

FIG. 3, 4, 5, 6 and 7 are from second experiment with subject A.

FIG. 3.—Volume 150 c.c., constant: 1, abdominal movement; 2, intrarectal pressure; 3, sensitive manometer showing vesical pressure via urethral catheter; 4, movement of perineum; 5, intravesical pressure by less sensitive manometer attached to ureteric catheter. At A the subject sighed. As soon as original vesical pressure of 5 cm. water was restored, a secondary wave, B, occurred in records 3 and 5 and reached 7 cm. pressure.

FIG. 4.—Constant volume, 100 c.c.; records as fig. 3. At A the subject commenced to think of micturition and allowed sufficient relaxation of the perineum to give him a sensation that micturition was possible, but did not encourage further relaxation. Note series of waves B, C and D, of vesical pressure, recorded by the two manometers.

FIG. 5.—Continuous with fig. 4, showing the effect of further encouragement of micturition by slightly further relaxing the perineum at fall of signal at A and subsequent lessening of effort, but no active restraint. At B the subject made a full effort to micturate, and at C restrained as strongly as possible. At D, termination of effort to restrain.

FIG. 6.—Follows fig. 5 on the orignal record. Attempt to micturate commenced at A, accompanied by perineal relaxation, followed by powerful restraint. More prolonged relaxation at B, and at C a "straining" movement of the abdominal wall. Further effort to micturate at D, and restraint at E. Small wave, F, at termination of restraint.

FIG. 7.—As fig. 6; voluntary effort to micturate at A, with effort to restrain at B; renewal of effort to micturate at C; a high-pressure response, D, before relaxation occurs after the effort to restrain at E.

FIG. 8.—The signal marks the abrupt commencement of sensation of distension. The volume had been constant at 400 c.c. for one and a half minutes. First experiment, subject A (see Plate II).

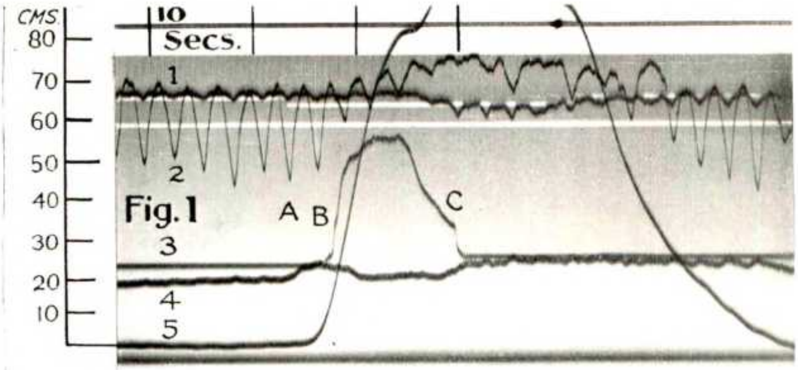


Fig. 1

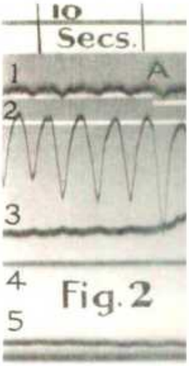


Fig. 2

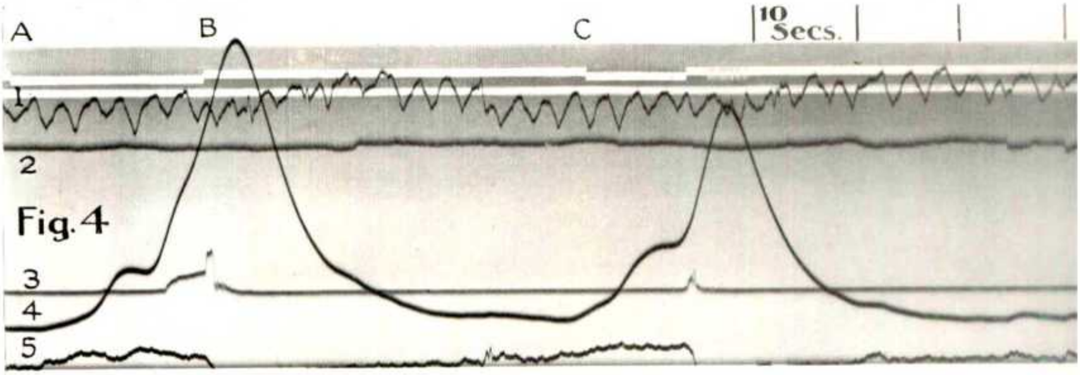


Fig. 4

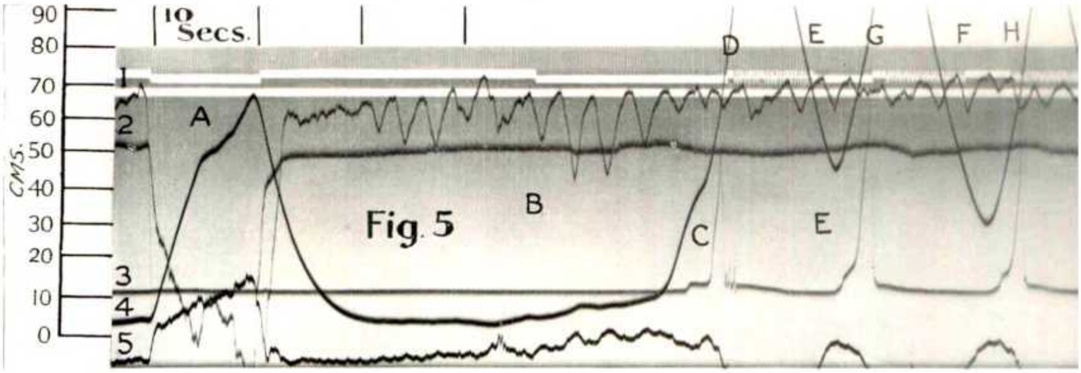


Fig. 5

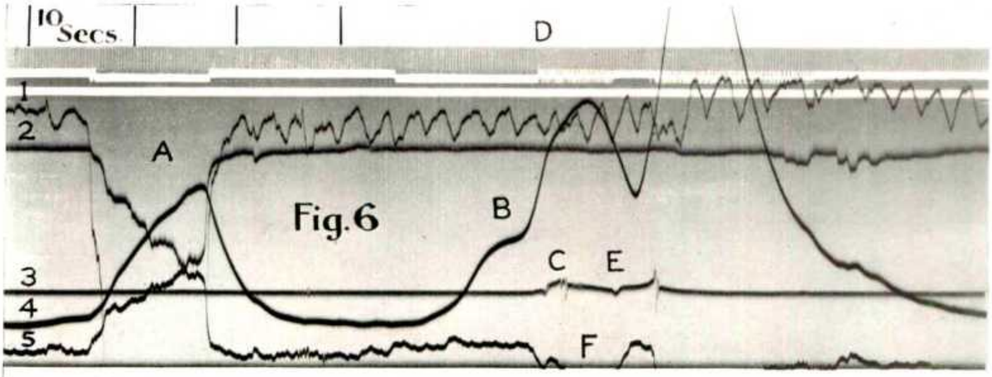
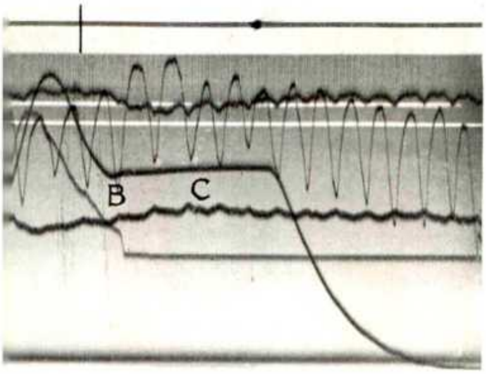


Fig. 6


B
C

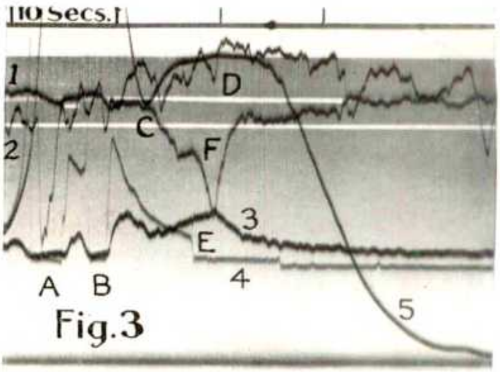
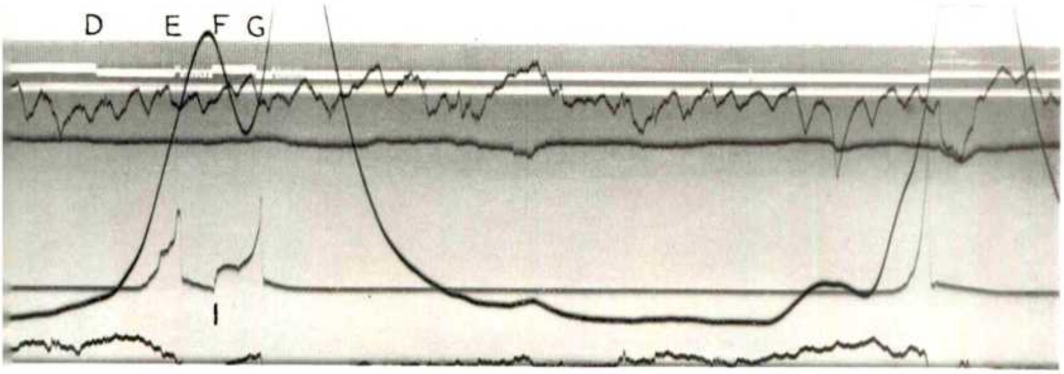

10 Secs.
1
2
C
D
F
3
E
4
A
B
5

Fig.3


D
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G
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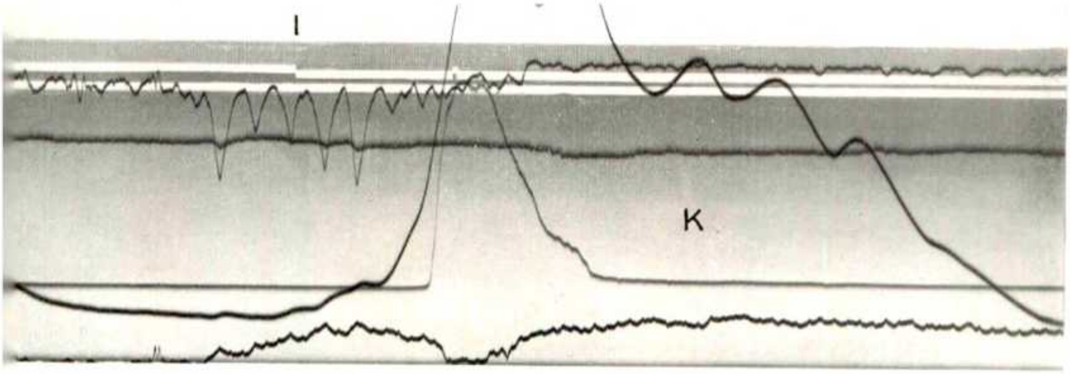
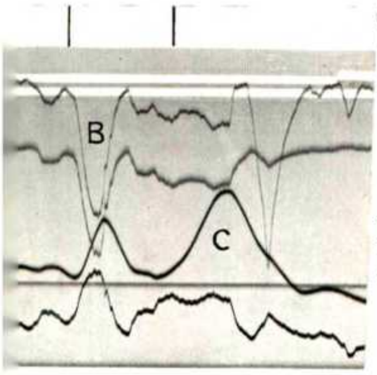

I
K


B
C

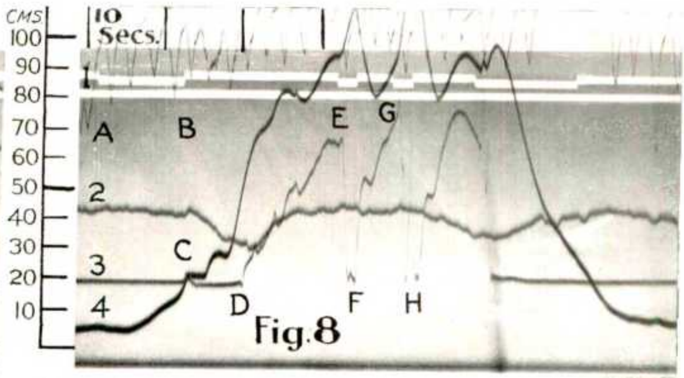

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Fig.8

## PLATE IV.

Micturition with catheters in dispositions shown diagrammatically in text, fig. 2 B and C. Figs. 1, 2 and 3, from third experiment on subject A with catheters as in text fig. 2 C. The tracings represent: 1, intra-rectal pressure: 2 abdominal movement; 3 in fig. 1, and 4 in figs. 2 and 3, pressure of outflow from catheter in urethra: 4 in fig. 1, and 3 figs. 2 and 3, movement of perineum; 5, true intravesical pressure by ureteric catheter. Vesical contents 50 c.c. at beginning of each figure.

FIG. 1.—Commencement of willed effort to micturate at A, with steep rise of vesical pressure, and opening of sphincter at B. Closure of sphincter, C, after approximately 50 c.c. had been evacuated. At C vesical pressure maintained high.

FIG. 2 as fig. 1, except that at B terminal contraction of bladder occludes the ureteric catheter and there is thus recorded a plateau (C) after the commencement of relaxation of vesical pressure before B.

FIG. 3, as figs. 1 and 2, but micturition interrupted by two brief willed efforts to restrain, A and B, and as the discharge lessens at C, the after-contraction D is fully recorded. Note sharp rectal contraction, F.

FIGS. 4, 5 and 6 from second experiment on subject A. Records: 1, abdominal movement; 2, rectal pressure; 3, pressure of discharge from sphincter; 4, vesical pressure; 5, perineal movement. In figs 4 and 5 urethral catheter lies beyond both sphincters; in fig. 6 its opening is between the two sphincters.

FIG. 4, volume 80 c.c.; A, commencement of effort, with onset of restraint at B. Repetition of same sequence at C, and at D another effort to micturate. Brief restraint E to F, and final restraint at G. Outflow aperture is slightly reduced between C and D. A response, restrained as in C, follows.

FIG 5.—As in fig. 4, with prolonged bearing down at A, but no relaxation of sphincter. Volume 80 c.c. Efforts to micturate at B, E, F, and I, and restraints at D, G, and H. The discharge after I is allowed to cease spontaneously.

FIG. 6 shows strain (A) and voluntary micturition (B), with effect of powerful restraint (D), the catheters arranged as in text fig. 2 B. Note delayed closure of sphincter at E, in spite of perineal contraction at F. Catheter moved slightly outwards after E.

FIG. 7.—A strain at B fails to open the sphincter in spite of the presence of waves of vesical contraction induced by a mild effort to micturate (A and C). Records as fig. 4, disposition as text fig. 2 B. Subject A, second experiment.

FIG. 8.—Vesical volume about 100 c.c. Subject A, first experiment. Numbering of records as fig. 4, but perineal movement is not recorded. Shows the involuntary brief closure of the sphincter immediately after the commencement of discharge, and subsequent voluntary restraints F and H, and the resulting change in vesical pressure. Note waves of positive intra-rectal pressure (of 8 cm. and 11 cm. water pressure).

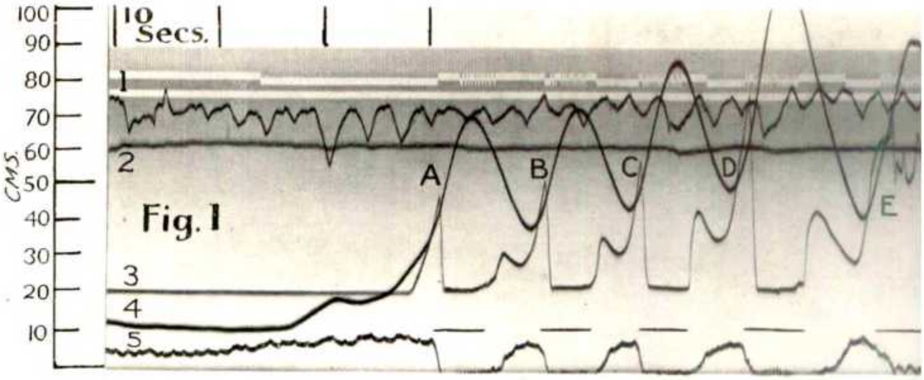


Fig. 1

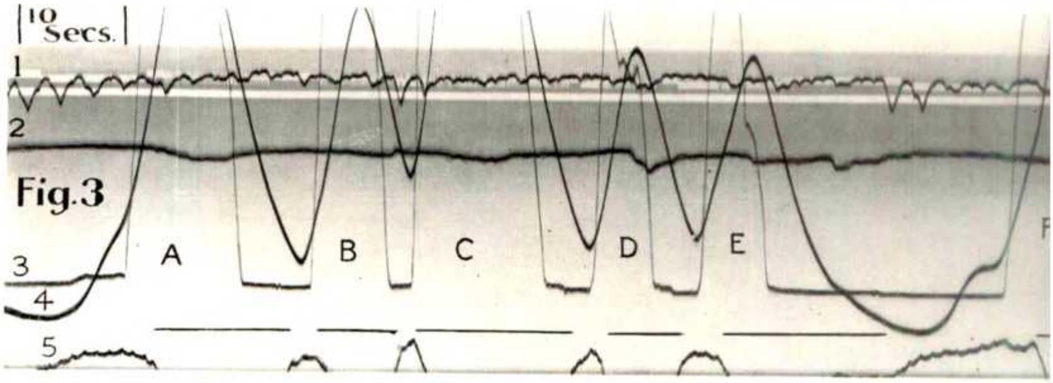


Fig. 3

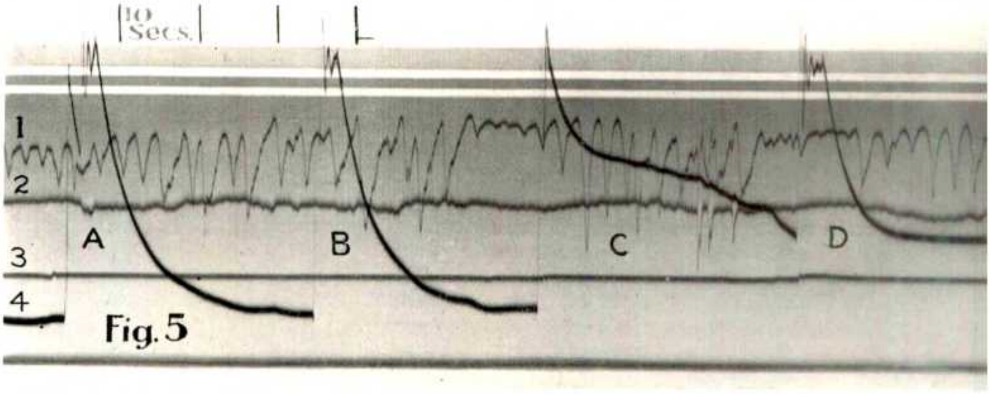


Fig. 5

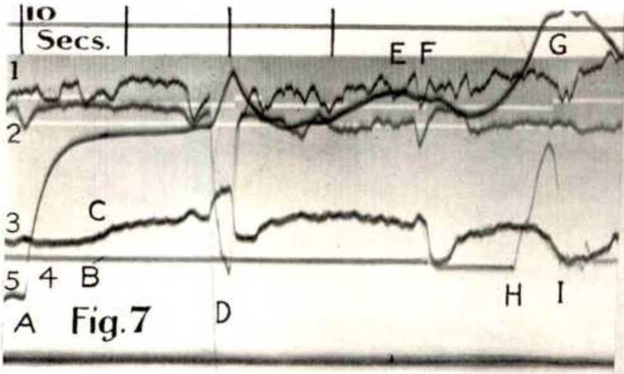


Fig. 7

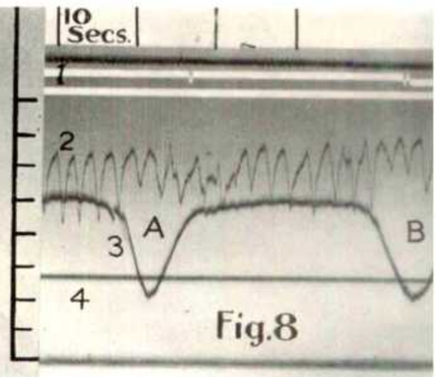
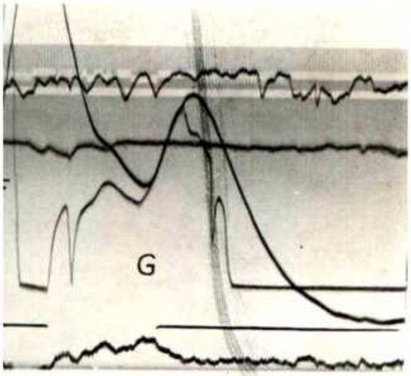


Fig. 8



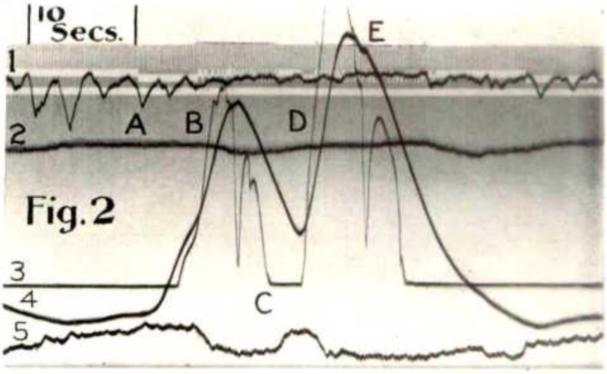
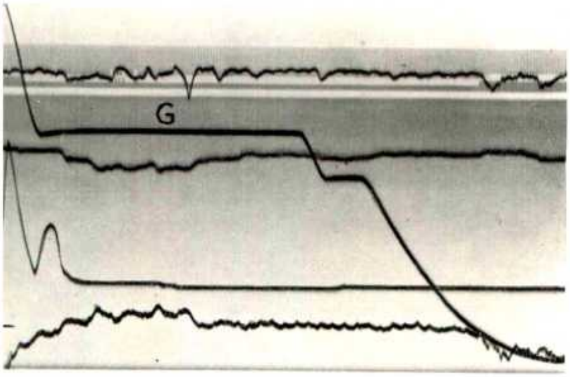


Fig. 2



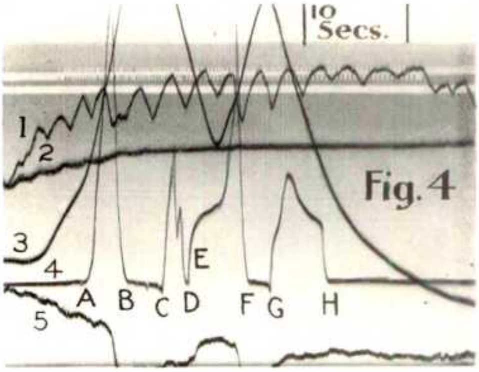
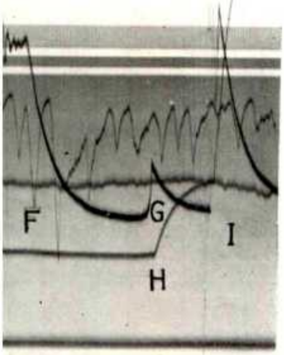


Fig. 4



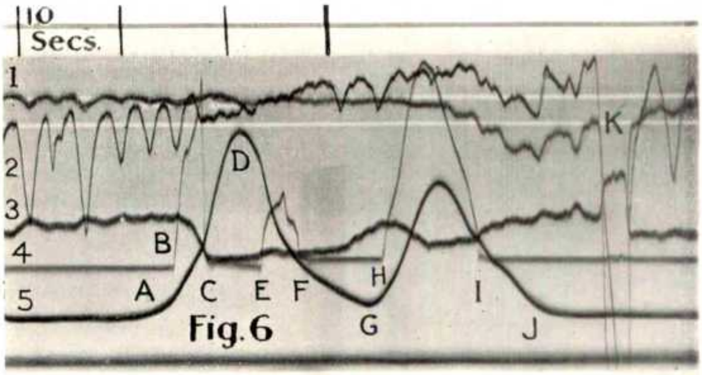


Fig. 6

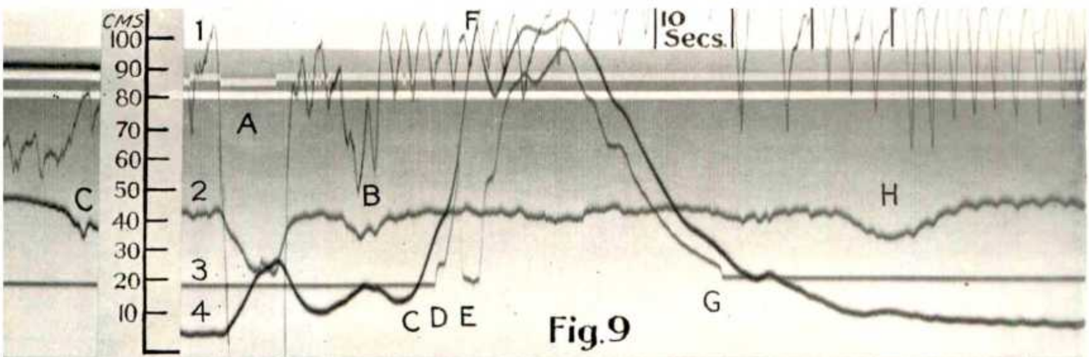


Fig. 9

## PLATE V.

FIGS. 1, 2, 3 and 4 from the second experiment on subject A. The numbering of the moving lines is the same as fig. 4, Plate IV.

FIG. 1.—Disposition of catheters midway between that in text fig. 2 B and 2 C. Vesical contents 60 c.c. Strong restraints of micturition (A, B, C and D) cause immediate cessation of discharge followed by delayed fall of vesical pressure. Milder effort to restrain causes delayed cessation of discharge (E and G). Horizontal line ruled above the perineal recorder indicates duration of each restraint.

FIG. 2.—Catheters advanced as in text fig. 2 B. Micturition commenced by effort at A, powerful restraint at B and E with delayed closure of sphincter. Volume 75 c.c.

FIG. 3.—Disposition as in fig. 2: initial volume 135 c.c. Strong efforts to restrain, duration marked as in fig. 1, each accompanied by relaxation of vesical contraction and delayed closure of sphincter. Rhythmical activity of the sphincter on closure, F. G, occlusion of the ureteric catheter by the bladder wall.

FIG. 4.—Disposition as in text fig. 2 C. The opening of the external sphincter C after restraint, occurs as the internal sphincter is about to close at D in reciprocation with falling vesical pressure. The renewal of vesical contraction is accompanied by relaxation of the internal sphincter. Willed external sphincter closure at F, reopening at G, and finally spontaneous closure at H.

FIG. 5.—Reservoir connected to pressure chamber of ureteric catheter and periodically the tap connecting the two is opened: 1, abdominal movement; 2, rectal pressure; 3, discharge through urethral catheter; 4, pressure in the pressure chamber of ureteric catheter. Volume of fluid in bladder 70 c.c. At commencement disposition as text fig. 2 C and catheters then gradually withdrawn. In A and B the fluid enters the bladder and the pressure falls rapidly after the injection; at C, D, E and F the fluid remains in the posterior urethra and leaks into the bladder only above the pressure required to force the internal sphincter. At G and I ureteric catheter is beyond external sphincter, and the fluid runs through urethral catheter at H.

FIG. 6. Disposition as in text fig. 2 D. Third experiment subject A. Volume of bladder 50 c.c. Both pressure chambers allowed to leak to sample pressure in two parts of the urethra. Willed micturition; relaxation of internal sphincter at A, of external at B. Willed restraint at C, relaxed again at E with terminal spontaneous closure at F. Further relaxation renews vesical contraction with late opening and early closure of the external sphincter (H, I). A strain, K, shows both sphincters are closed. The lag of the ureteric catheter system tends to smooth over abrupt events.

FIG. 7.—Record follows on fig. 6. Reservoir inflow attached to ureteric pressure chamber. Fluid run into posterior urethra at high pressure at A. No escape from external sphincter even with effort to micturate at B, or a brief strain at D. Continued effort causes full micturition with normal relaxation of the external sphincter at H, closed by restraint at I.

FIG. 8.—3, records intra-rectal pressure (moves downwards with increase); 2, abdominal movement; and 1, pressure of inflow to bladder (100 cm.) during a slow filling through ureteric catheter, Two independent waves of pressure within the rectum at A, B. Pressure in rectal balloon shown on scale on left in divisions representing 10 cm. water. Initial pressure 40 cm.

FIG. 9.—Record, as in Plate IV, fig. 8, of micturition with vesical contents between 100 and 150 c.c. Involuntary restraint at E and effect on vesical pressure (F). Terminal spontaneous closure at G, probably of external sphincter. Isolated rectal contraction at H.

# PARENCHYMATOUS CORTICAL CEREBELLAR ATROPHY (CHRONIC ATROPHY OF PURKINJE'S CELLS).[1]

BY HARRY L. PARKER, M.B.DUB.
(*Section on Neurology,*)
AND
JAMES W. KERNOHAN, M.B.BEL.
(*Section on Pathologic Anatomy,*)
*The Mayo Clinic, Rochester, Minnesota.*

## INTRODUCTION.

IT is by no means easy to obtain a clear understanding of all that is included under the term cerebellar atrophy. In the literature available on the subject are many poorly organized reports dealing both with the clinical aspect and the pathological findings after death. Assumptions based on deficient anatomical inquiry go hand in hand with the most meticulous pathological research of material lacking all or almost all clinical features. Classifications based on a mixture of clinical and pathological factors and without criteria to guide their destiny appear in every article on the subject, and to a student commencing his labours they end in producing a state of confusion. Each writer on the subject of cerebellar atrophy has added his quota, and from the maze of types a few classifications remain that are helpful. Reference might be made to classifications by Mingazzini, Holmes, Archambault and the more recent one of Marie, Foix and Alajouanine. Each system of classification has been based on the sum total of knowledge acquired at the time it was made, plus certain ideas of the writers. To attempt a more modern classification, however, considering how far short knowledge of the subject of cerebellar atrophy falls, would result simply in further confusion. A few types of cerebellar atrophy remain nevertheless, and serve as outstanding examples, for the simple reason that in each instance the work of their delineators, including both clinical and pathological features, is reasonably adequate and satisfying. The progressive familiar type of cerebellar degeneration described by Holmes, the olivo-ponto-cerebellar atrophy of Dejerine and Thomas, and a type of cerebellar atrophy recently described by Marie, Foix and Alajouanine, serve as shining examples. The last-named type is the basis of the present consideration; it has been described by various observers in the past, and by virtue of its simplicity and clarity is entitled to fair consideration. Throughout the years since the first description by Murri in 1900 the type has been known by many names. Murri called it cerebellar degeneration due to intestinal intoxication, and recent writers on the subject, Kirschbaum and Eichholz, in 1932, described it under the caption of cerebellar cortical atrophy. Throughout this period of thirty-two years, fifteen cases have been described. Perhaps the most lengthy account of the disease was given by Marie, Foix and Alajouanine in 1922 with the somewhat lengthy name of primitive parenchymatous atrophy of the cerebellum of cortical localization. No matter how the names have varied from writer to writer, the clinical and pathological syndromes seem to have been essentially the same. Recently a case of this type of cerebellar atrophy has come under our observation and since relatively few cases have been reported in literature, and these mostly in foreign literature, we have deemed it advisable to review the subject again, and to record our experience, and our rather guarded views with regard to the ætiology. For purpose of clarity, the title of our contribution has been adapted from the English nomenclature and the name of the disease (parenchymatous cortical cerebellar atrophy) approximates closely that used by the American writer, Archambault.

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[1] Read before the Chicago Neurological Society, Chicago, Illinois, April 20, 1933.

Fifteen cases have been recorded by various observers. The widespread distribution of patients shows that no local factor can be responsible. Thus, one patient lived in Italy, ten patients lived in France, three in Germany and one patient in the United States. Since anatomical confirmation was lacking in two cases described by Rossi and in one case described by Marie, Foix and Alajouanine, these are excluded from consideration, especially since various diseases in the cerebellum may give a similar clinical picture. Another case described by Marie, Foix and Alajouanine is excluded for the reason that clinical data were lacking, and the case represented merely a pathological specimen of unknown origin. In one of Rossi's cases the findings at the necropsy were not mentioned, but it was included because later Marie, Foix and Alajouanine described the same patient who had since come to necropsy. Thus eleven cases remain that are representative of the essential characteristics of a disease, intriguing because of the simple clinical syndrome noted during life, and the clear-cut conditions in the cerebellum noted after death.

## CLINICAL CHARACTERISTICS.

In the cases recorded there did not appear to be any familial tendency, thus contrasting with the group of cases described by Holmes. Further, no other disease seemed to occur in the family that might have a bearing on the problem except in the case of Kirschbaum and Eichholz in which the families in the three preceding generations had been heavy drinkers of alcohol. The sex of the patient was recorded in nine of the eleven cases reviewed. Seven patients were males and two were females. The age of onset of the disease was after middle life in most cases. Nine patients were aged between 40 and 80 years, and the average age was 62, somewhat more advanced than the average of 57 given by Marie, Foix and Alajouanine. Two cases in the series, however, were different in respect to age at onset of disease. The patient described by Archambault had a severe illness characterized by gastro-intestinal disturbances and fever at the age of 17. Thereafter his upper and lower extremities were awkward and clumsy. Nevertheless, he was able to work and these difficulties did not increase until he reached the age of 40, when a slow and steady progression of ataxia occurred. In the case described by Kirschbaum and Eichholz progressive cerebellar ataxia developed slowly and insidiously; commencing at the age of 20 and progressing to the patient's death at 59. However, this condition was not very not noticeable until the age of 35. He was first in hospital at the age of 41 when he sought relief for his condition. He continued his employment as clerk until the age of 46 when he was pensioned, mainly because his handwriting became illegible. These two cases, therefore, differ markedly from the others in the age of onset and the life history of the disease. In most cases the disease appeared for the first time between the fifth and seventh decades and, therefore, after the prime of life, and when regressive changes are beginning to be manifest.

The mode of onset is usually gradual and insidious, the disease involving the body symmetrically, progressing steadily and slowly over a period of years to helplessness and death from intercurrent disease. The two cases of Murri and of Rossi are exceptions to this course. In Murri's case the disease was primarily acute with gastro-intestinal symptoms, and it ran a relatively rapid course to a fatal termination within nine months. In Rossi's case the condition came on acutely following diarrhœa; it improved after three months, only to relapse again into a more slowly progressive form over a period of eight years. Stender and

Lüthy's patient had had a stormy initial episode characterized by acute polyneuritis of alcoholic origin. This cleared in five months, leaving residual ataxia, which was stationary for fifteen years, but later progressed to a fatal ending. Excluding Murri's case, in which the course was unusually rapid, the average length of illness among the ten other patients was $13\frac{8}{10}$ years, constituting a chronic, long-drawn-out course.

The chief complaint of all the patients, as might be expected, was difficulty in walking. From descriptions of complaints and the clinical picture it would seem that the ataxia was of a relatively pure type, and that associated with cerebellar disease. The lower extremities were always much more seriously involved than the upper, at least in the earlier stages of the disease before the patient became completely helpless and bedridden. The gait was swaying and hesitating, with oscillations antero-posteriorly, compared by many observers to the staggering, reeling progression of an intoxicated man. The legs were spread wide apart to give firmer support, and often the trunk did not follow the progress of the legs so that the patient tended to pitch forward or backward. The hands were held to grasp at support, and many patients were forced to use canes, crutches or the support of a friendly arm. Some patients who fell could not arise without help, but once balanced they could stand alone. Various tests of the lower extremities with the patient lying or sitting showed dysmetria and dyssynergia, commensurate with the stage of the disease. An element of spasticity in the lower extremities was described by Kirschbaum and Eichholz, Jelgersma and Rossi, but this was never marked and was dominated largely by the cerebellar features.

In six of the eleven cases recorded the upper extremities were relatively unaffected in the disturbance of function so marked in the lower extremities. Marie, Foix and Alajouanine made a point of this and drew some interesting conclusions concerning cerebellar function by noting the corresponding site and distribution of the more severe lesions in the cerebellum itself. However, in five cases severe inco-ordination of the upper extremities was noted, and they were as functionally impaired as the lower extremities. The more severe examples of this involvement of the upper extremities are represented by the cases of Kirschbaum and Eichholz, Archambault and Jelgersma. Jelgersma stated that his patient spilled water when he raised a glass of it to his lips, could not untie a knot once he had tied it, and his handwriting, a specimen of which was shown, was almost illegible.

Although it is hard to separate clinically a so-called tremor from the oscillations produced by cerebellar disease, apparently none of the patients had anything like a violent shaking of the limbs as might be seen in a disease such as multiple sclerosis. Jelgersma and Archambault described tremor of the head, again apparently part of the syndrome of cerebellar disturbance. The speech was affected in seven cases, and was variously described as being monotonous, drawling, slow, staccato and explosive; generally it was indistinct. In two cases it was apparently unchanged, and in two cases this function was not mentioned. Nystagmus was not marked in any of the cases; at the most there were a few unsustained jerks of the eyes on lateral deviation. In all cases the disease was symmetrical and equal on both sides of the body. An outstanding feature was the preservation of intelligence in all the cases reviewed and this persisted to the end. The actual cause of death of these patients was sought, since it is obvious the disease itself should not be lethal. In four cases the terminal state was not mentioned. Pneumonia occurred in two cases; chronic bronchitis, cardiac failure, carcinoma of the pancreas, cirrhosis of the liver and apoplexy were given as causes of death in the remainder of the cases.

### PATHOLOGICAL DATA.

In most cases gross atrophy of the cerebellum was reported. Archambault described the cerebellum as being reduced by a third, and Rossi found it reduced by a fourth and a fifth in two cases respectively. In two cases of Marie, Foix and Alajouanine it was diminished by a quarter. Stender and Lüthy, Lhermitte, Kirschbaum and Eichholz, and Thomas also mentioned that the cerebellum was smaller than normal, but the amount of reduction was not estimated. Nevertheless, in one case of Marie, Foix and Alajouanine and in Jelgersma's case, the volume of the cerebellum was described as being normal. Therefore, there seems to be no uniformity in this respect, and it is manifestly difficult to estimate by ordinary methods gross alteration in size of the human cerebellum.

In cases in which there was obvious atrophy, closer examination, particularly in the cases of Marie, Foix and Alajouanine disclosed widening of the sulci and both shrinkage and hardening of the individual foliæ. This also seemed to have a particular distribution according to intensity. It was more marked in the vermis and particularly in the supero-anterior portion. These changes diminished laterally and posteriorly so that the parts least affected in the cerebellum were the posterior and inferior portions of the vermis and the more lateral portions of the lateral lobes. Thus, although the entire cerebellum may be affected, the superior vermis and quadrilateral lobule receive the brunt of the disease.

Microscopical examination showed first, under low-power magnification, that the atrophy was confined to the cortex, and except for minor changes in the white matter of the individual foliæ, the central white matter of the cerebellum as well as the dentate and other roof nuclei were normal. Under higher power the outstanding lesions of the disease were revealed, namely, a relative or absolute disappearance of the Purkinje cells, according to the area examined, with preservation of the basket structures around them. On this fundamental point all authors are agreed, and it may be seen that the disappearance of so large and conspicuous a structure as the layer of Purkinje's cells gives a characteristic appearance to the sections of the cerebellar cortex. The distribution of this destruction of Purkinje cells corresponded to the gross changes mentioned, that is, more intense in the region of the superior vermis and quadrilateral lobule. In these areas the Purkinje cells were absent. In other areas changes occurred signifying varying degrees of destruction with swelling, karyorrhexis, diminution in the intensity of the stain, eccentricity of the nucleus, and shrinkage, and finally only shadows of the cells remained prior to their complete disappearance.

The cortex, under moderate magnification, appeared to be thinned. The breadths of the granular and molecular layers were diminished, they stained less intensely and there was slight proliferation of neuroglia. The white matter of the folia appeared to be slightly rarefied, and according to Marie, Foix and Alajouanine it was sclerosed and this sclerosis ended with a line of demarcation where the white matter of the folia met the central white matter of the cerebellum. The latter structure was normal microscopically. More minute study by Bielschowsky's method and other silver stains showed the entire wiping out of the Purkinje cells with their plumes. The basket cells, climbing fibres, mossy fibres and T-shaped fibres were everywhere preserved. As a contrast, the plexus of fibres above and below the Purkinje cells, considered by Cajal as being retrograde collateral fibres, were, in conformity with this idea, absent. Marie, Foix and Alajouanine described atrophy and sclerosis of the postero-medial portion of the inferior olivary nucleus and mild degeneration of the olivary fibres. Stender and Lüthy also noted these changes. All other parts of the central nervous system were normal. With the exception of Archambault, all authors reported

PLATE VI.

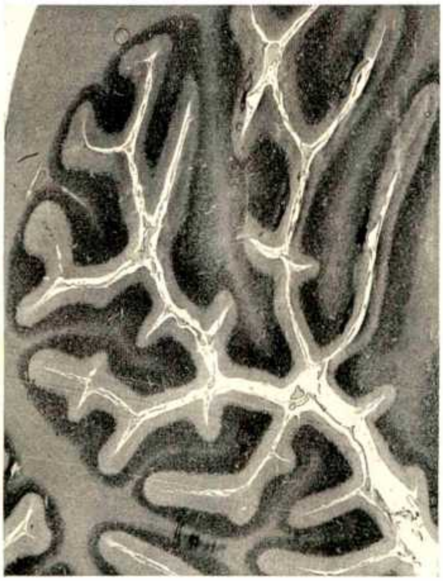

FIG 1.

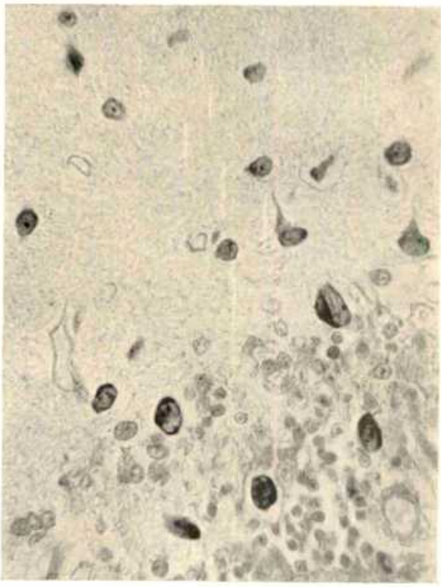

FIG. 2.

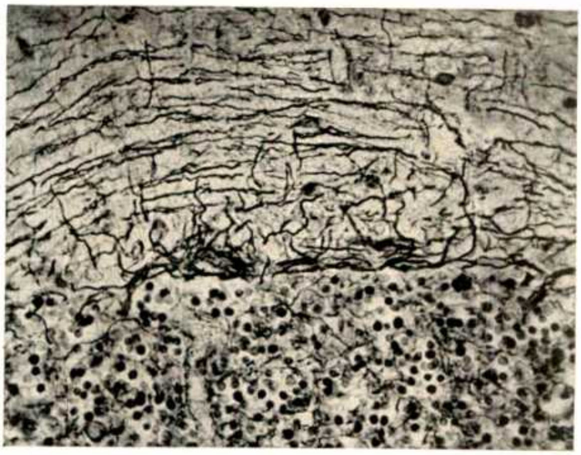

FIG. 3.

FIG. 1.—Gross atrophy was not present. The molecular and granular layers are intact. and there is no atrophy of the white matter. Meningitis was not present and the blood-vessels were normal (hematoxylin and eosin, × 8).

FIG. 2.—Several immature ganglion cells may be noted in close proximity to the Purkinje cell layer. The cells do not have dendrites or axis cylinders, but they have the characteristic nuclei and nucleoli as well as Nissl granules. Normal Purkinje cells are absent (thionin, × 550).

FIG. 3.—Absence of Purkinje's cells may be observed, but the baskets are well preserved. Tangential fibres in the molecular layer and also fibres in the granular layer may be noted (modified Orlandi silver impregnation method, × 300).

*To illustrate Paper by Parker and Kernohan.*

PLATE VII.

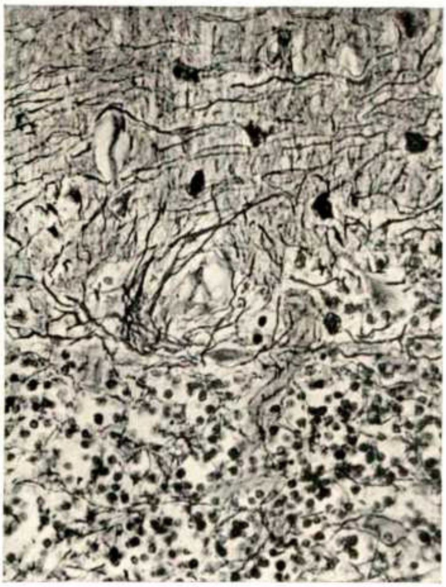

FIG. 4.

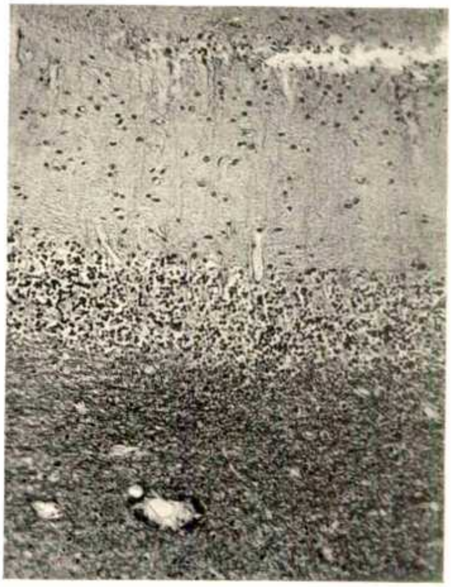

FIG. 5.

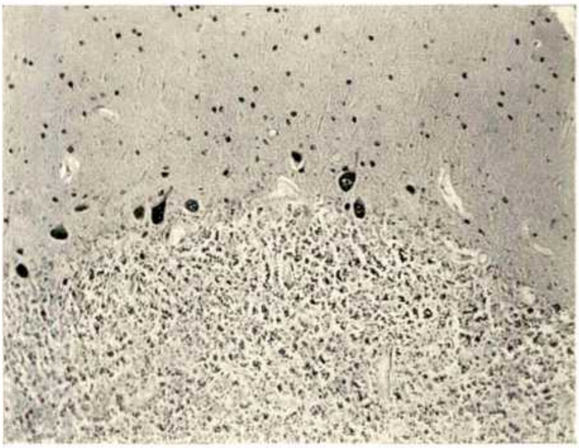

FIG. 6.

FIG. 4.—The remnants of a degenerated Purkinje cell with well-preserved basket may be noted. There are numerous fibres in the molecular and granular layers (modified Orlandi silver impregnation method, × 400).

FIG. 5.—An increase of glial fibrils in the molecular layer may be noted; definite gliosis is present in the white matter, especially around the blood-vessels. Purkinje's cells are absent and there is slight atrophy of the granular layer (Mallory's phosphotungstic acid hematoxylin, × 140).

FIG. 6.—A few of the Purkinje cells remaining. They are slightly atrophic, with few dendrites, slightly irregular in distribution, but contain normal Nissl substance. Atrophy of the molecular or granular layers is not present, and the blood-vessels are normal. There is no sign of any inflammatory process (thionin, × 115).

*To illustrate Paper by Parker and Kernohan.*

the meninges and blood-vessels as normal. Archambault described thickening of the meninges and blood-vessels, and emphasized these changes as being of possible causal connection.

The cerebellum therefore may be normal or atrophied to the naked eye; if atrophied the foliæ are shrivelled and the sulci widened according to a certain distribution. Microscopically, the one constant change is massive destruction of the layer of Purkinje's cells with preservation of the basket cells. Other changes are slight, inconstant and seem of little importance. Actually, therefore, the disease seems to be one in which for some reason there is specific destruction of a certain layer of cells in the cerebellar cortex and preservation of all other structures. The case reported herewith represents one more example illustrative of this specificity, and the elective affinity of the disease for the cells of Purkinje.

## REPORT OF CASE.

A woman, aged 58, was brought to The Mayo Clinic, September 6, 1930, because of inability to walk. There was no history of a similar condition in her family. At the age of 28 she had had influenza and at 38 she had been confined to bed for several weeks because of nervousness and exhaustion. A diagnosis was made at that time of bronchitis. Six years before admission she had fractured her left tibia. Twenty-one months previously she had fallen for no apparent reason and fractured her left wrist. About the time that she fell she had noticed progressive weakness and exhaustion, and unsteadiness of gait. She lost weight, became nervous and was very depressed mentally. Six months previously her unsteadiness had been quite noticeable and she was sent to a hospital for a rest. She returned to work in about ten days, but her difficulties were even more marked. Four months previously she noticed that she had poor control of the use of her hands; she commenced to spill her food, writing became increasingly difficult, and finally she was unable to feed herself. She had been bedridden for three months prior to her examination at the clinic. Changes in her speech had occurred five months previously, and this had been progressive to the point where she was understood with difficulty. Her mental depression became more marked, and finally she became quite helpless.

At the time of examination the patient was pale and emaciated. She weighed 100 lb.; her normal weight was 117 lb. The systolic blood-pressure was 122, the diastolic 88 in millimetres of mercury. The pulse was 94 and during the period of eight days' observation remained about that level; there was no fever. Speech was slow and scanning. Pelvic examination disclosed a nodular, hard mass extending halfway to the umbilicus. The specific gravity of a single specimen of urine was 1·015; it was acid in reaction and contained a large number of pus cells, but no albumin or sugar. Concentration of hæmoglobin was 77 per cent. Erythrocytes numbered 4,050,000 and leucocytes 8,400 in each cubic millimetre of blood. The Wassermann test on the blood was negative. The pupils of the eyes, the reflexes, the visual fields and the fundi were normal. Movements of the eyes were slow and incomplete, and the patient had difficulty in holding the eyes in extreme lateral rotation. There was no definite nystagmus. Roentgenograms of the thorax disclosed an old calcified apical tuberculous lesion on both sides; those of the cervical part of the spine and of the skull were negative. There was no muscular paralysis at any time and all sensations were preserved. The tendon reflexes were all active, the abdominal reflexes were preserved and Babinski's sign was not present. The finger-to-nose test and finger-to-finger test disclosed marked inco-ordination of both upper extremities, somewhat more marked on the left side. When the patient was assisted by two persons she was able to walk a few steps, swaying helplessly to either side or pitching forward. The movement of her limbs in walking was irregular, inco-ordinate and showed marked dysmetria. This inco-ordination and dysmetria were also quite marked in both upper extremities. Dysdiadokokinesia was present and marked. The Wassermann reaction of the spinal fluid was negative; the value for total protein was 20 mg. in each 100 c.c., the globulin test was positive, and there was one small lymphocyte in each cubic millimetre. The colloidal gold curve was 55444100000. The colour and the physical properties of the fluid were normal and it was under pressure of 30 c.c. of water. The pressure of the spinal fluid responded promptly to compression of the jugular veins.

The patient became steadily worse in the hospital. She vomited and became weaker. A diagnosis was made of progressive cerebellar degeneration (type unknown), bilateral calcified pulmonary tuberculosis and large pelvic tumour. She was sent home with the expectation that the terminal event would soon occur. However, she lived six months, about twenty-seven months from the presumed onset of her trouble, after her return home. She was unable to feed herself and she was practically helpless. Difficulty of speech increased, and from time to time she had attacks of fever. Ten days before death pain developed in the thorax, a friction rub could be heard and her temperature was 102° F. Necropsy was performed, and through the kindness of the pathologist the brain and spinal cord were sent to us, as well as a complete report of other findings.

The essential cause of death in this case was apparently a bilateral carcinoma of the ovary which had extended into the regional and peri-aortic lymph nodes. It had metastasized into the liver and lungs, and the lymph nodes of the hilum contained innumerable masses of varying sizes with necrotic centres. Evidence of extensive bronchopneumonia was present in the posterior portions of the lower lobe of both lungs. There were no findings of significance in the other organs of the thoracic and abdominal cavities.

The brain and spinal cord had been removed intact and reached us in excellent condition in solution of formaldehyde. To the naked eye no lesions of any part of the nervous system were apparent. There was no atrophy of the cerebellum and the foliæ seemed to be of normal size (Plate VI, fig. 1). There was no arteriosclerosis of the vessels of the circle of Willis or of any other vessels. The meninges were not thickened, nor was there any turbidity. The cerebrum was cut by coronal sections but evidence was not found of hydrocephalus, infarcts, or metastatic tumours. The mid-brain, pons and medulla appeared normal.

Sections were taken from all parts of the nervous system, including cerebrum, cerebellum, brain-stem and spinal cord and also the meninges. The stains used on these sections were Weigert myelin sheath, hæmatoxylin and eosin, thionin and the Orlandi modification of Bielschowsky silver impregnation method. Since the brain had been fixed in solution of formaldehyde, the gold chloride and sublimate method of Cajal and the silver carbonate method of Rio Hortega could not be carried out, and Mallory's phosphotungstic acid hæmatoxylin stain was used for glial fibrils.

Microscopically the various sections disclosed: (1) The meninges and blood-vessels were normal. (2) An excess of lipochrome pigment was noted in the anterior horn cells of the spinal cord, but there was no degeneration in these cells. There was no degeneration of any of the tracts and sclerotic plaques were absent. (3) There were no changes in the axis-cylinders, myelin sheaths or glial cells of the medulla oblongata, pons and mid-brain. In the olivary nuclei of the medulla oblongata there was an excess of pigment in many of the ganglion cells which were otherwise normal. The pigment was usually in the form of minute granules, but they were sometimes quite large. All had an affinity for silver but did not react specifically for iron. Weigert's myelin sheath stain did not show degeneration in any of the tracts of the medulla and brain-stem, including the olivary connections. There were several small groups of vacuoles near the olivary nuclei, the nature of which could not be accurately determined. There were no findings indicating inflammatory reaction. (4) Sections were taken from various portions of the cerebral cortex; there was no chromatolysis or pyknosis of any of the ganglion cells, but many of the larger pyramidal cells contained an excess of pigment which had an affinity for thionin stain and for silver. This was more marked, however, in the cells of the basal nuclei, where every cell contained pigment, but again there was no other sign of degeneration. (5) Microscopical preparations were made from numerous areas of both cerebellar hemispheres, the vermis and dentate nuclei. The outstanding condition was diffuse destruction of the

Purkinje cells with preservation of the basket cells. Sections taken from the different portions of the cerebellar hemispheres and vermis were examined separately and the findings compared.

In the inferior border of the left hemisphere the hæmatoxylin and eosin stain did not disclose signs of old or recent meningitis or any inflammatory condition, and no scavenger cells or evidences of phagocytosis were noted. In the molecular layer there appeared to be a slight increase of cells in scattered foci, but this increase was not general. Many of the nuclei of these cells seemed to be astrocytes, but some were large and vesicular with a deeply staining central nucleolus. The molecular layer was of normal thickness and was neither atrophic nor hypertrophic. There was no pigment and no rarefaction of the tissues in this zone. There was no decrease or increase in the number of cells in the granular layer so that it was neither atrophic nor hypertrophic although the nerve-fibre layer was normal. With the thionin stain those cells in the molecular layer which had large vesicular nuclei, and deeply staining nucleoli were seen to be very small ganglion cells. There was a narrow ring of cytoplasm, containing numerous fine granules of Nissl substance surrounding the nuclei (Plate VI, fig. 2). These cells did not have any dendrons and most of them were rounded, although occasionally the Nissl granules collected into several masses giving the cells a pyramidal or polygonal shape. None of these cells was bipolar, and all seemed to be differentiated and mature. In the Purkinje cell layer all ganglion cells had disappeared although occasional faint traces of degenerating ones were visible. Pyknotic cells were not present. There were no small ganglion cells similar to those seen in the molecular layer. All the cells of the granular layer were normal, except some small ganglion cells similar to those seen in the molecular layer. These were scattered throughout the granular layer but were more common near the Purkinje cell layer. There were no large ganglion cells like Purkinje cells in the layer. With the Orlandi modification of the Bielschowsky impregnation method the small ganglion cells in the molecular layer did not have dendrites or axis-cylinders, although they did have an affinity for silver. In the deeper part of the molecular layer, there were many normal axis-cylinders lying parallel to the surface of the convolutions; these were not beaded or fragmented. Close to the Purkinje cell layer there were some very fine axis-cylinders projecting into the molecular layer; these belonged to the processes of the basket cells. Although the Purkinje cells had disappeared leaving no trace practically all the baskets surrounding the disintegrated Purkinje cells were intact. In spite of the complete absence of normal Purkinje cells and their processes, the surrounding basket fibres were intact and normal (Plates VI and VII, figs. 3 and 4) with numerous processes and fibrils just as if the Purkinje cells were present. All the baskets were intact, but some were better seen than others. There were innumerable axis-cylinders running in all directions in the granular layer and some entered the nerve-fibre layer. All the axis-cylinders of the granular layer and the nerve-fibre layer were normal; there was no apparent diminution in numbers, and there was no degeneration. The axis-cylinders in the nerve-fibre layer were parallel to each other, and there was absence of beading, swelling and fragmentation. Mallory's phosphotungstic acid hæmatoxylin stain showed that there were many neuroglial fibrils running at right angles to the pia mater in the outer two-thirds of the molecular layer. The inner third was devoid of such gliosis. Most of the Purkinje cell layer was also devoid of glial fibrils, although occasionally small clusters were present. There were more fibrous astrocytes in the granular layer than normal, and there was a marked gliosis in the nerve-fibre layer. This formed a denser mat than is normal and was pronounced around the blood-vessels, especially around the large vessels (Plate VII, fig. 5).

In the lateral portions of the left hemisphere findings similar to the foregoing were present in the molecular layer, and a smaller number of similar cells were present in the superficial part of the granular layer. There was a slight increase in the astrocytes in the molecular layer. There was no rarefaction in the Purkinje cell-layer, and no Purkinje cells were present in the molecular or granular layers. All the other tissues were normal. There was no old or recent inflammation in any of the layers of this part of the cerebellum.

In the superior border of the left cerebellar hemisphere, findings were also similar to those of the inferior and lateral borders, except that some Purkinje cells were undergoing chromatolysis. No normal cells were found. In the molecular and granular layers close to the remnants of the Purkinje cells there were fewer small ganglion cells. Axis-cylinders undergoing active degeneration were not found. In the inferior and lateral borders of the right hemisphere there was complete absence of Purkinje's cells and the other findings were identical with those of the left hemisphere. However, in the superior border of the right hemisphere close to the vermis there was a considerable number of well-preserved Purkinje's cells. In several foliæ there were Purkinje's cells, normal both in numbers and structure except that an occasional cell was out of alignment and was situated in the lower third of the molecular layer. The other layers of the cerebellum, superficial and deep to these cells, were normal. In the outer portions of several foliæ there were normal Purkinje cells, and in the deeper recesses of the foliæ they had completely disappeared. The transition between these two portions was abrupt (Plate VII, fig. 6). There was no demonstrable reason for the abrupt change; the blood-vessels in each portion were normal, there was no sign of old or recent inflammation, and the other layers of the foliæ were normal. The baskets were present and equally well preserved in both portions. In such folia there were no small ganglion cells in the molecular or granular layers, but there seemed to be a slight increase in the number of glial cells in the molecular layer.

The inferior vermis was similar to the other portions of the cerebellum, and the Purkinje cells were absent. The only difference was an increase in the number of small ganglion cells which were more numerous in, and scattered diffusely through, the granular layer.

The superior vermis was similar to the inferior vermis, except that occasional normal Purkinje cells were present. Several small areas (portions of several folia) retained normal Purkinje cells which seemed to survive in small segments of the foliæ, and the junction with their adjacent portions where the ganglion cells had disappeared was abrupt.

The ganglion cells of the dentate nuclei were intact, but most of these cells contained excessive pigment which was frequently collected into coarse granules and had an affinity for silver, but did not react specifically for iron. Some cells had disintegrated, as occasional granules of this pigment were lying free in the stroma or in the perivascular spaces. Cells were not undergoing chromatolysis, but an occasional cell appeared to be pyknotic. There was a zone of rarefaction surrounding both dentate nuclei which appeared spongy. The vacuoles seemed to be the result of numerous swollen oligodendroglial cells. Besides this zone of rarefaction there was an excess of astrocytes which was most marked in the hilum of the dentate nuclei. Mallory's phosphotungstic acid hæmatoxylin stain showed that most of the astrocytes were of the fibrous type, with numerous neuroglial fibrillæ. There was no sign of recent or old inflammation in or around the dentate nuclei. Weigert's myelin sheath stains did not show degeneration of the myelin around the nucleus even where the zone of rarefaction was noted.

The blood-vessels in all parts of the cerebellum were normal. There was no evidence of arteriosclerosis, and the perivascular spaces were not dilated, and no cells or products of degeneration were present.

## COMMENT.

Clinically the case recorded here is comparable with cases reviewed in the literature. The onset of the disease was insidious, as is usually the case. The patient dated her troubles from the time when she fell and fractured her wrist. It is probable that her balance was not quite normal at the time. Her age was about 56 when symptoms commenced; about the average age when the disease usually commences. The course was unusually short, lasting only twenty-seven months, in contrast to the more chronic cases reported. Complete helplessness was reached within a few months; the case therefore resembles the single case of Murri in which the disease ran its complete course from onset to death in eight months. There was no dissociation between involvement of lower extremities and the disturbance in the upper extremities. The ataxia and inco-ordination were universal and involved the movements required for articulation also. In six of the total twelve cases the patients were similarly affected, thus in 50 per cent. of the cases the disturbance of the upper extremities approximated that of the lower extremities.

As usual there was no nystagmus, suggesting clinically a lesion confined to the cerebellum and leaving the vestibular nuclei or their corresponding tracts in the brain-stem intact. There was nothing of the violent movement tremor seen in multiple sclerosis, and the sphincters were unaffected. As is usual also, the patient's intelligence was unimpaired.

In considering the diagnosis in this case there were some extraneous factors that finally turned out to be more associated than causal. The patient had an old pulmonary tuberculous lesion, and a pelvic tumour of uncertain nature. Tuberculoma of the cerebellum or metastatic carcinoma to the brain was considered, but finally rejected because of lack of corroborative evidence. Nevertheless, they were the confusing details of the clinical findings. Multiple sclerosis was also considered as is so often the case in these diseases, but was rejected because of the age of the patient and the purity of the cerebellar syndrome. Finally, no other conclusion could be reached than that the disease was a progressive degenerative process in the cerebellum.

With regard to the influence of the carcinoma on the disease, one can only assume that in the main it constituted a terminal event; it is possible that the cachexia and weakness resulting from it exaggerated the general functional impairment and helplessness. The disease comes on at a time in life when the incidence of carcinomatous changes is high and at least one other patient, described by Lhermitte, suffered similarly from carcinoma of the pancreas that caused death. Like the pulmonary tuberculosis, the carcinoma probably had no causal connection, although it made the diagnosis more difficult.

If our case resembled in its main clinical features the characteristics of the cases reported in the literature, the resemblance in pathological detail was much more close. As always, the predominant feature was the diffuse and massive destruction of the Purkinje cells with preservation of the basket cells. It is true there was no gross atrophy and the disease in question has been called cerebellar atrophy. Nevertheless, in a case of Marie, Foix and Alajouanine and in the case of Jelgersma, the cerebellum was normal in size. This, however, does not preclude atrophy which is cellular and specific for one type of cell, and at the same time is unassociated with diminution of the gross volume of the cerebellum. It is possible that a more slowly progressive process causes greater shrinkage in size due to secondary sclerotic processes. Nevertheless, Jelgersma's patient had the disease eight years before death. Similar to the other cases there were no striking changes elsewhere in the nervous system, as the various tracts connecting the cerebellum with other structures were entirely normal. Some minor changes were observed, and for the sake of completeness will be given some consideration.

The diffuse pigmentary change in many of the ganglion cells throughout the central nervous system must be considered abnormal. With advancing age there is normally an increase of lipochrome pigment in many ganglion cells and frequently in most of them, but in this case it was in excess of that usually seen in persons of an age similar to this patient. The significance of an excess of pigment is unknown, but the consensus of opinion considers it a sign of wear and tear or a degenerative phenomenon, but there is no evidence to suggest that the presence of this melanin-containing pigment interferes with the function of the cell. Usually the pigment granules are minute and the melanin portion has an affinity for silver, as was noted in this case, whereas the lipoid part has an affinity for fat stains and the pigment gives a polychrome reaction with thionin. In some cells, especially in the dentate nucleus, the small granules had fused into larger ones, which could readily be seen with a lower power microscope, and occasionally there were free granules indicating complete disintegration of the cells. These granules were free in the glial spaces and occasionally in the perivascular spaces, but there was no evidence that phagocytosis had taken place, and there was no activity of the microglial or other scavenger cells.

There was absence of any general glial reaction, and that around the dentate nuclei was sharply localized for which there is no satisfactory explanation. It could scarcely be a post-mortem phenomenon on account of its sharp demarcation, and there was not sufficient degeneration of the ganglion cells to account for the reaction of the oligodendroglia or the astrocytes. The pigmentary degeneration of the ganglion cells of the dentate nuclei was more advanced than that observed in any other group of cells in the central nervous system, and this may be the result of the disappearance of the Purkinje cells. The similar but less severe changes in the ganglion cells of the olivary nuclei may be accounted for on the same basis. In spite of the pigmentary changes the ganglion cells of both the dentate and olivary nuclei had retained their functions as the axis-cylinders and their accompanying myelin sheaths were intact.

The disease from which the patient died has been referred to as cerebellar atrophy, yet in most cases, and in our case in particular, there was no gross evidence of atrophy, and the degeneration was sharply limited to the Purkinje-cell layer, and practically all the other changes noted microscopically were secondary to this. The presence of very small and apparently immature ganglion cells in the molecular and granular layers might be interpreted as an attempt at regeneration or formation of new cells to replace the Purkinje cells that were destroyed. If this is the explanation of the presence of these small cells, such a phenomenon is unique in the central nervous system. The slight increase of astrocytes in the Purkinje-cell layer should be regarded as a replacement phenomenon and we did not consider it the primary lesion. Altogether the changes found under the microscope and apart from the destruction of the Purkinje cells seemed unimportant and could hardly have led to any marked impairment of function.

## GENERAL COMMENT.

So far, we have considered the results of observation and have dealt with facts. Proceeding thence to hypotheses as to the causation of the disease, we are treading on much less certain ground. The uncertainty lies in the lack of uniformity of antecedent phenomena in the disease. Marie, Foix and Alajouanine had covered all the possible ætiological factors up to the time of their publication. They emphasized two main factors, namely an early infectious process antedating the appearance of the disease, and its late onset in the life of the patient. They invoked a double pathogenesis, and suggested that a previous infection or toxic process had injured a poorly endowed Purkinje-cell system leading later to premature decay. The element of infection or intoxication is necessary as well as an abiotrophic condition of the cell. Archambault also suggested an antecedent infectious process as cause, but it acted on the meningeal vessels and determined a slowly progressive atresia of these cells leading in later life to cortical atrophy from malnutrition. Unfortunately for this latter hypothesis, the majority of observers has failed to find significant lesions in the vascular system supplying the cerebellar cortex.

If an infectious origin is assumed, the case of Murri showed a fair basis for this hypothesis. The disease began with severe gastro-enteritis which persisted during most of the subsequent events, and the patient died after being ill only eight months. Symptoms developed in a case of Rossi fifteen days after the patient had had severe diarrhœa that persisted for six weeks. This patient died of cirrhosis of the liver. Stender and Lüthy, however, were satisfied that chronic alcoholism was the main cause, and certainly they had reason, as the patient had had delirium tremens three times and his cerebellar difficulties commenced following severe neuritis caused by alcohol. Kirschbaum and Eichholz also believed alcoholic excesses were to blame, for though the patient had never indulged, for three generations his family had been heavy drinkers of alcohol. It was assumed that this heritage led to a system poorly endowed with Purkinje cells, so that at the age of 20 spontaneous degeneration developed and continued until the patient's death. Thomas's patient had had syphilis, alcoholism, typhoid fever, otitis media and probably acute anterior poliomyelitis. So many antecedent illnesses make the problem here too complex for direct argument as to cause and effect.

Unfortunately, there is a negative side to the picture. There is an appreciable number of cases on record, including those of Jelgersma and Lhermitte, in which the past history of the patient gave no indications of infection or intoxication. Our patient had had influenza thirty years before the onset of her symptoms, but it was not particularly severe and was merely mentioned when the history was being taken. Anyone reaching an age between 50 and 70 years had a good chance of having had at some time in life some type of mild or severe infection. To associate this with a disease appearing many years later required a large amount of proof. Nevertheless, exceptions to this can be found in other diseases of the nervous system as will be mentioned. To presume that a patient is constitutionally predisposed to a disease without a familial or hereditary history of the disease is also begging the question. It may be necessary to approach the problem from a different angle.

Since the outstanding feature of the disease is a progressive selective deterioration of the Purkinje cells and relative conservation of the other elements in the cerebellum, it might be asked whether there is any reason for assuming that the cells are particularly weak in middle age and later. There are some observations tending to support this assumption. The Purkinje cells are present at birth but underdeveloped and immature in form. There is then rapid growth during the first six months, but they do not reach full size until from twelve to eighteen months after birth. Later acquired structures in the central nervous system are usually the first to disappear during senescence and disease. Ellis found that there is a gradual loss of Purkinje cells with advancing age. This begins normally at about the age of 40 and gradually progresses as time goes on. As well as actual disappearance of cells, degenerative changes also occur in those that remain; chromatolysis, atrophy, vacuolation and homogenous degeneration of the nucleus and cytoplasm and pigmentary changes were found in the Purkinje cells of old age. Moreover, the regions most affected were those most injured in cortical cerebellar atrophy. The cells of the dentate nucleus were much less affected in senescence. Inuka found the same senile degeneration of the Purkinje cells in albino rats, but not to the same degree as in human beings.

The progressive changes in the Purkinje cells that occur after the age of 40 might indicate a relatively increased vulnerability of these cells as compared with other portions of the cerebellum, more especially in later life. The question also arises as to whether in the more well-known types of progressive cerebellar atrophy occurring just before or after middle age, the Purkinje cells are badly affected. This is actually the case in the olivo-ponto-cerebellar atrophy described by Dejerine and Thomas, the olivo-rubro-cerebellar atrophy of Lejonne and Lhermitte, and particularly in the type of familial degeneration of the cerebellum described by Holmes. In the latter disease the Purkinje cells of practically the whole cortex except the tonsils, the uvula and the nodule are severely affected, and this destruction of Purkinje's cells is the most conspicuous change in the cerebellar cortex. Again a local selectivity of disease appears, in that the degeneration of the Purkinje cells is most severe in the superior vermis, the flocculus and the pyramid. In these types of cerebellar degeneration of adult life other structures are badly injured, but the Purkinje cells receive more than their share of injury. Accordingly, the thesis might be advanced that in adult life, especially after the fifth decade, the Purkinje cells are more readily affected by age and disease than the rest of the cerebellum, and have a relatively high degree of vulnerability.

From the standpoint of histological changes the disease in question might represent the influence of endogenous or exogenous toxins, of some unknown type of disease or so-called degeneration as yet not understood. There is no evidence of acute or chronic inflammation, although such may have at one time appeared and disappeared without leaving a trace of its previous existence. Inorganic toxins such as lead have been known to injure the Purkinje cells, as the experimental work of Ferraro and Hernandez has shown, but this injury is not specific for the cells and exerts its influence elsewhere in the nervous system. Alcohol has been suggested by Stender and Lüthy as the essential cause in their case. Considering the common use of alcohol there ought to be a higher incidence of the disease, but actually it is quite rare. An endogenous toxin is an improbable cause, since there is no obvious source for it and no indication of its action elsewhere in the body. To call the condition a degenerative disease opens the question as to what caused the degeneration.

Recently, attention has been drawn to the problem of changes of tissue in virus diseases, notably by Ledingham. Acute types, such as acute anterior poliomyelitis, are well known, but as yet our knowledge of chronic forms of such disease is limited. Cases have been recorded of chronic disease of the anterior horn cell commencing anew and progressing to a fatal termination years after an episode of acute anterior poliomyelitis was over. Oppenheim described clinically a chronic anterior poliomyelitis that may appear without any antecedent history of infection. Homologous to this is chronic bulbar palsy, in which the cells of the motor nuclei of the bulb disintegrate. These diseases, moreover, are more prone to occur in the later decades of life. At necropsy little is found outside of the specific destruction of cells. Epidemic encephalitis may be followed by a chronic progressive Parkinsonism which may appear ten years or more after an initial encephalitis and progress to a fatal termination. Of recent years cases of this chronic disease have been observed in which there is no history of epidemic encephalitis, or perhaps of mild influenza or a common cold. In some of the chronic cases no change is found after death other than progressive destruction of the cells of the basal ganglia and substantia nigra. All evidence of acute or chronic encephalitis had disappeared long since. It is, therefore, not impossible that parenchymatous cortical cerebellar atrophy is in some instances at least due to a virus disease. It may be introduced into the body during some previous infection, lie dormant throughout the years, and then fasten on to the Purkinje cells at an age when they are least resistant. Thus is started a slow, remorselessly progressive disease, ending in helplessness and death.

Support for these ideas as to causation would be manifest if there existed an acute specific disease of Purkinje's cells of virus origin, as occurs in the anterior horn cells of the spinal cord. In human beings such a condition is of extremely rare occurrence. There is, however, an acute virus disease affecting animals and destroying specifically the Purkinje cells. This disease occurs in epidemic form in sheep, and is confined apparently to some counties in the north of England. It has been called "louping-ill" and is transmissible to mice and monkeys [2, 6]. Hurst produced the disease in four monkeys, and it was characterized by progressive cerebellar ataxia. At necropsy, a more or less diffuse encephalomyelitis was present, accompanied by massive destruction of the Purkinje cells of the cerebellum. Hurst drew attention to the analogy between this disease and acute anterior poliomyelitis.

In the final analysis as to the cause of the disease in the group studied, it is probable that more than one factor is to blame. Chronic alcoholism may be the cause in one group of patients. Among patients whose difficulties are beginning at an advanced age, premature senescence of the Purkinje cells might be suggested, especially as it is known these cells tend to decay in advance of other cells. Among younger patients with a history of somewhat more rapid onset, and with an antecedent or parallel infectious or toxic process, a virus disease with a specific affinity for the Purkinje cells might be considered. Finally, as is usually the case, there may be a group of cases in which clues as to the essential cause are lacking and the ætiology is unknown.

## SUMMARY AND CONCLUSIONS.

The clinical and pathological characteristics of parenchymatous cortical cerebellar atrophy have been outlined. Hypotheses have been expressed as to the cause of the disease. The histological findings at necropsy are characteristic, and readily recognizable. Clinically, the

## SUMMARY OF DATA.

| Author and year | Age, years and sex | Duration of disease years | Previous illness | Involvement | Tremor | Speech | Cause of death | Gross appearance of cerebellum | Comment |
|---|---|---|---|---|---|---|---|---|---|
| Murri .. .. 1900 | 59 F. | ¾ | Gastro-enteritis | General | Hands | Slow, hesitating | Cardiac failure | Not mentioned | Rapid course |
| Thomas.. .. 1905 | 40 F. | 19 | Typhoid, syphilis, alcoholism; anterior poliomyelitis | Trunk and lower extremities | Lower extremities | Nasal (gumma of palate) | Chronic bronchitis | Normal | Claw feet; extensor plantar reflexes, spastic toward end |
| Rossi .. .. 1907 | 59 M. | 9 | Diarrhœa | Lower extremities | Hands | Spasmodic | Cirrhosis of liver | Atrophied | |
| Archambault .. 1918 | 17 M. | 48 | Typhoid | General | Head and extremities | Slow, monotonous nasal | Pneumonia | Atrophied; reduced by ⅓ | Some rigidity legs and arms; early onset |
| Jelgersma .. 1919 | 30 M. | 8 | None | General | Head and arms | Slow, explosive | Not mentioned | Normal | |
| Lhermitte .. 1922 | 67 M. | 13 | None | Lower extremities | None | Not mentioned | Carcinoma of pancreas | Atrophied | |
| Marie, Foix and Alajouanine 1922 | 68 ? | 14 | None | Lower extremities | None | Slow | Not mentioned | Atrophied; reduced by ¼ | |
| Marie, Foix and Alajouanine 1922 | 62 ? | 6 | None | Trunk and lower extremities | None | Normal | Not mentioned | Atrophied; reduced by ¼ | |
| Marie, Foix and Alajouanine 1922 | 60 M. | 5 | Unimportant | Trunk and lower extremities | Lower extremities | Drawling, monotonous | Not mentioned | Atrophied | |
| Stender and Luthy 1931 | 60 M. | 10 | Chronic alcoholism: delirium tremens; alcoholic polyneuritis | General | Arms | Monotonous; indistinct; ataxic | Broncho-pneumonia; senility | Atrophied | |
| Kirschbaum and Eichholz 1932 | 20 M. | 39 | Acute rheumatic fever | General | Arms | Staccato, slow, indistinct | Apoplexy; pneumonia | Atrophied | Early onset |
| Parker and Kernohan 1933 | 58 F | 2 | Influenza | General | None | Slow; scanning | Carcinoma of ovary | Normal | Rapid course |

disease represents a slowly progressive cerebellar syndrome, beginning after middle age in both men and women. The diagnosis need not be very difficult except when separating the clinical syndrome from other types of cerebellar degeneration. The failure to obtain a history of heredofamilial characteristics and the relative purity of the cerebellar syndrome are of assistance in the latter respect. Arteriosclerosis with infarction of the cerebellum produces a clinical course that is abrupt and intermittent, and lacking the smooth progressive course of the disease outlined. The disease usually begins before senile changes are manifest, and the preservation of the intellectual faculties distinguishes it from a general senile breakdown of the nervous system.

The disease is rare; only twelve cases, including our own, have been recorded in which necropsy has verified the identity of the process. Interest in the condition is created by the observation of a clear-cut clinical syndrome and a specific destruction of cells in the cerebellum. We hope that this study will lead to a better understanding of the mechanism that underlies not only the physiologic reactions to disturbed cerebellar structure, but to the factors involved in cellular pathologic changes.

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# THE LOCALIZING SIGNIFICANCE OF SPASTICITY, REFLEX GRASPING, AND THE SIGNS OF BABINSKI AND ROSSOLIMO.

BY MARGARET A. KENNARD, M.D., AND JOHN F. FULTON, M.D.
*(Laboratory of Physiology, Yale University School of Medicine, New Haven.)*

IN Babinski's original description [1] of the pathological plantar reflex published in 1896, he stated that the reaction consisted of simple extension of the toes. In 1903, however, he observed [2] a second component of the response, *i.e.*, fanning and lateral deviation of the toes, which "in certain cases," especially in familial diplegias, accompanied the simple extensor reaction. Since then the extensor phenomenon has been clearly established as pathognomonic of pyramidal tract lesions, but the significance of the fanning sign in relation to localization has not, so far as we are aware, been given serious consideration. Fulton and Keller [10] in their study of the Babinski response in chimpanzees observed fanning in several instances following lesions of motor projection areas of the cortex, and more recent observations, which we propose now to record, indicate that the phenomenon is not associated with lesions of the pyramidal tracts.

The present study is based largely upon the chimpanzee, and in particular upon four tame specimens in which various cortical lesions were made. Corroborative evidence drawn from the monkey, baboon and gibbon, has been included where relevant, but these forms are less well suited for the problem in hand since they exhibit fewer of the common pathological reflexes of clinical significance (Fulton and Keller [10]; Schick [20]).

## THE "MOTOR" AREAS OF THE CORTEX.

Cortical lesions restricted to Area 4 of Brodman [4, 5], *i.e.*, to the classical motor area from which the pyramidal tracts take origin (fig. 1), give rise in the chimpanzee and apparently in all other primates, to a simple, and for the time being complete, *flaccid* paralysis [10, 11]. Within a few weeks after such a lesion, however, the animal recovers volitional power in all muscles except those governing the finer movements of the digits. Spasticity has never been seen in the affected extremities following such an extirpation, except as a transient phenomenon in a few instances.

When the premotor area (Area 6 of Brodman) is destroyed (fig. 1) in primates a different picture is seen, *i.e.*, there is transient loss of voluntary power in the contralateral extremities [14, 6], but the paresis is accompanied by an increased resistance to passive manipulation, and the limbs become *spastic* [10]. In addition, involuntarily reflex grasping occurs, as was first demonstrated experimentally by Richter and Hines [17, 18] (see also [9]). Both these phenomena disappear, usually in a few days, and the ultimate motor performance of both the monkeys and chimpanzees is on the whole normal, though a curious reluctance to initiate voluntary movements may persist indefinitely [14].

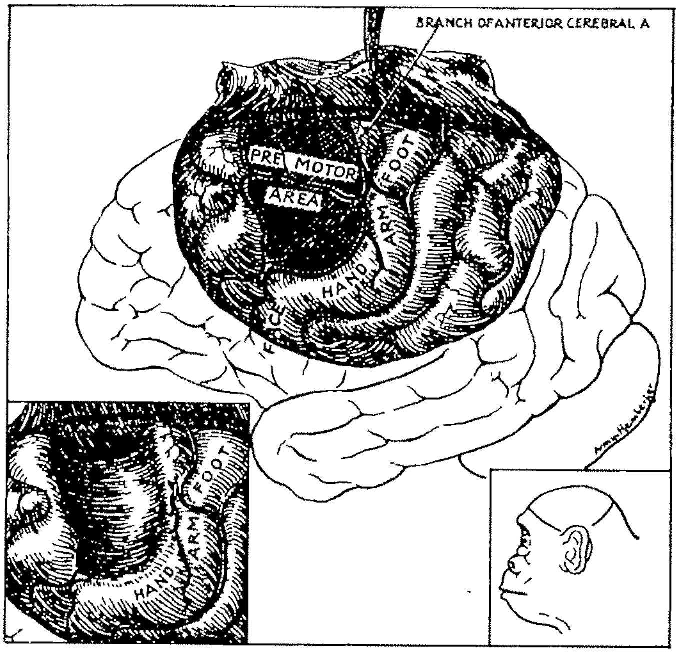

FIG. 1.—Left hemisphere of a chimpanzee (Experiment 4) showing the motor cortex (Area 4) from which the arm area was extirpated April 19, 1932, and the premotor cortex (Area 6) extirpated November 11, 1932.

If, from a chimpanzee in which Area 4 has been destroyed,[1] the premotor region of the same side is removed at a second operation, the opposite extremities again lose voluntary power completely, and become immediately *spastic*, exhibiting lengthening and shortening reactions, the "clasp-knife" phenomenon, &c. Recovery of voluntary power in the small muscles of the digits does not occur, though gross flexion and extension movements of the larger joints may be regained, the ultimate residual deficit is far greater in all muscles than that which follows isolated extirpation of Area 4 or Area 6 alone [11]. The spasticity and correspondingly greater motor deficit also occur when Areas 4 and 6 are removed simultaneously. It is evident, therefore, that the presence of spasticity, in the chimpanzee, and probably in man, has definite localizing value in the study of cortical lesions, especially when considered in relation to the pathological reflexes discussed below.

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[1] Full details concerning the results in monkeys of successive removal of Areas 4 and 6 from both hemispheres in various combinations have been reported by the present authors in another paper [11, 12].

## EXPERIMENTAL MATERIAL.

The four animals on which the study is based may now be briefly described. All surgical procedures were carried out under sodium amytal anæsthesia, except for the fourth operation in Experiment 4, in which ether was used. For each operation a bone flap was turned down and ultimately replaced with all precautions that one ordinarily employs for a similar operation on man. (See Fulton and Keller [10].)

A detailed study of pathological reflexes other than the Babinski in various primate forms has been made recently in this laboratory by Schick [20] who has established in the chimpanzee the responses homologous with the signs of Chaddock, Oppenheim, Schaffer, Gordon, Rossolimo and Mendel-Bechterew in man. For elicitation of these responses in chimpanzees we have followed the procedures which he has described. Attention may be directed again to the fact that the signs of Rossolimo and Mendel-Bechterew which are exaggerated "deep" reflexes, *i.e.*, tendon responses of the digits, fall into a group quite separate from the cutaneous Babinski, Chaddock and Oppenheim responses. Flicking the tips of the toes, or tapping the digital tendons near the metacarpophalangeal joints serve as the adequate stimulus for the Rossolimo reflex [19].

*Experiment* 1 ("*Yama*"). *Male chimpanzee weighing* 17,300 *grm. Successive removal of Area* 4 (*foot*) *from both hemispheres at intervals of six weeks followed in each instance by flaccid paralysis and Babinski response without fanning. Subsequent removal nine months later of Area* 6 (*left*),

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[1] Weights indicated in these four experiments are as of April, 1933.

*followed by strong contralateral spasticity, loss of voluntary power, forced grasping, pronounced and permanent Rossolimo's sign and the fanning sign of Babinski.*

The subject of the experiment was a well-trained and co-operative chimpanzee, the early history of which has been fully described elsewhere (Fulton and Keller [10], Experiment 16). The foot areas were identified by faradic stimulation and removed, one on January 21, 1932 (left) and the other on March 4, 1932. In each instance the lesion, restricted to Area 4, gave rise to a striking flaccid paralysis of the opposite hind limb with depression of deep and superficial reflexes for a period of several days after each operation. The Babinski phenomenon was at first sluggish, but it increased gradually in amplitude during the first week, and after the second operation ultimately became equal on the two sides and readily obtained. For a period of eight months thereafter it remained constant. The response was unassociated with the fanning sign of Babinski, and the signs of Rossolimo and Mendel-Bechterew, though present immediately after the operation, were never marked. Forced grasping could not be evoked. The gradual return of voluntary power in all muscles, except the digits, has been previously described [10].

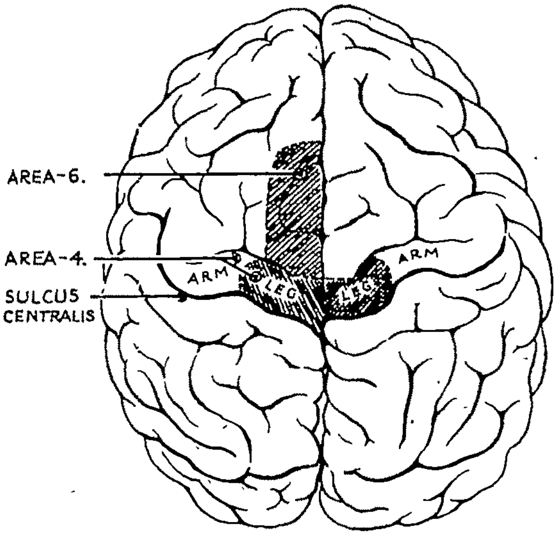

FIG. 2.—Drawing of the cerebral hemispheres of a chimpanzee (Experiment 1) showing the left motor foot area extirpated January 21, 1932, the right motor foot area extirpated March 4, 1932, and the left superior premotor area extirpated December 6, 1932.

*Removal of left premotor area.*—On December 6, 1932, the superior part of the left premotor area was removed under sodium amytal anæsthesia (fig. 2). On recovery from anæsthesia the animal had a markedly spastic right hind limb which within less than forty-eight hours began to show: (1) The fanning sign of Babinski with great increase in the ease of elicitation of the sign of

Babinski itself; (2) involuntary forced grasping of hand and foot—that of the hand passed off after ten days, but in the foot, provided the body was in the maximal position for the grasp reflex (see Bieber and Fulton [3]), it could still be demonstrated at the end of four months; (3) a pronounced Rossolimo response obtainable with a slight stimulus. The spasticity and impairment of motor power diminished somewhat after six weeks, but the fanning, forced grasping and a pronounced Rossolimo reaction have persisted (four months), and bid fair to be permanent. At present (April, 1933), the animal shows the following signs: In the right lower extremity a positive Babinski, Chaddock, Rossolimo, Mendel-Bechterew and a general motor deficit which is markedly accentuated by fatigue. There is also slight spasticity and forced grasping and the fanning sign of Babinski which is not present in the left foot. On the left, the Babinski and Rossolimo are positive, but less easy to elicit and less well marked than on the right. There is no forced grasping or spasticity, and motor function on the left is far better than that on the right.

*Experiment* 2 ("*Boy*"). *Young male chimpanzee weighing* 13,600 *grm. Successive removal of Area* 6 *from both hemispheres, followed in each case by forced grasping, transient spastic paresis, marked impairment of spontaneous motor performance and permanent Rossolimo with modified fanning sign, but absent Babinski.*

This animal, a young and tame male chimpanzee, has been trained by Dr. C. F. Jacobsen in problems [14] requiring skilled movements of the hands and fingers. On December 9, 1932, the left premotor area (Area 6) was removed. Forced grasping immediately became prominent in both right extremities and persisted for about ten days, gradually disappearing as voluntary prehension returned to hand and foot. With the forced grasping there was an increase in resistance to passive manipulation of the right extremities, and a state of spasticity which appeared to cause the right extremities to be moved slowly and less readily than the left, and to be held in a characteristic semi-flexed posture when the animal was at rest. During the first two days after operation a jerking extensor response to plantar stimulation occurred on the right and was accompanied by a flaring of the smaller toes. After the second day, this response was always flexor in type and was accompanied by lateral deviation of the toes. The sign of Rossolimo was elicitable in the right at first but disappeared after two weeks. The right knee-jerk was more active than the left, immediately following operation.

At a *second operation* (January 9, 1933), Area 6 was extirpated from the right side. Immediately following the operation, the *right* extremities became markedly *spastic*; the left were flaccid during the first post-operative day, but then became very spastic also. Extreme spasticity was present for nearly two weeks, but after this it gradually became less and disappeared at the end of the third week. During the first weeks forced grasping was present in all four extremities, disappearing gradually as the spasticity became less and persisting longer in the hands than in the feet.

The plantar reflexes again became extensor in type on both sides during the first post-operative day, but exaggerated plantar flexion supervened on the second day and has persisted three months, associated with the fanning sign, *i.e.*, there is lateral deviation of the toes in addition to the flexion response. The deep reflexes, *i.e.*, knee-jerks, were exaggerated. The Rossolimo reflex returned on the right in more pronounced form and it also appeared on the left, and has persisted permanently on both sides.

At present (April, 1933), no motor deficit can be detected and the performance of the animal appears normal, but the knee-jerks continue hyperactive and the Rossolimo sign, although less marked, is still easy to elicit bilaterally. The plantar responses are exaggerated flexor in type on the right but they have become variable and difficult to elicit on the left side.

*Experiment* 3 (*"Sambo."*)—*Mature male chimpanzee weighing* 38,000 *grm. Radical removal of entire premotor area from left hemisphere, followed by spasticity, forced grasping, signs of Rossolimo and fanning and transient Babinski.*

The animal had been in the laboratory for six months and had also been trained on problem boxes. On January 3, 1933, the entire left premotor area was removed (fig. 1), the excision being deeper and more radical than in Experiment 2, but it did not impinge on Area 4. A profound right motor deficit ensued with extreme spasticity and forced grasping which still persisted after six weeks, although it had gradually become less pronounced.

An extensor Babinski response was present on the right side during the first eight days, and was accompanied by a flaring and lateral deviation of the digits which has persisted but the extensor response of the digits has disappeared. The Rossolimo sign was observed to be positive on the sixth post-operative day and has persisted in well-marked form for three months.

Subsequently (April 24, 1933) the right premotor area was also removed which caused re-appearance of forced grasping on both sides and the Rossolimo sign was permanent on both sides. At a third operation on June 2, the entire motor area above the face was destroyed on the left side, after which the extremities became highly spastic and have remained in this condition until the present time (July, 1933).

*Experiment* 4 (*"Mussai"*).—*Male chimpanzee weighing* 24,200 *grm. Removal of both arm areas* (*Area* 4) *and both premotor areas* (*Area* 6 *entire*) *at four successive operations. Permanent forced grasping in arms. Permanent Rossolimo and transient fanning of toes, but no Babinski.*

The subject of this experiment was a young male chimpanzee which had been trained on box problems during a period of eight months prior to its first operation. On April 19, 1932, the left motor cortex representing the arm was removed, and on May 15, 1932, the corresponding area was removed from the right motor cortex. After each operation, flaccid paralysis of the contralateral arm occurred followed by gradual recovery of function, but with permanent impairment of movements of the digits. There was no impairment of motor function of either lower extremity. After the first operation a slight and transient Rossolimo appeared in the right foot, but disappeared completely on the eighth post-operative day.

No other pathological reflexes of the lower extremities were demonstrated until the *third operation* (November 11, 1932) when the entire *left* premotor area was removed (fig. 3). Spasticity of the right arm with very marked forced grasping of that hand appeared at once and both symptoms persisted, although in recent months they have tended to become slightly less pronounced. Very slight and transient spasticity of the right leg was also evident, with slight involuntary groping and grasping which disappeared ten days later.

On January 16, 1933, at a *fourth operation*, the right premotor area was removed. Marked spasticity of both upper extremities appeared with moderate increase in resistance to passive manipulation, especially of the left extremities. Forced grasping was also marked, and became permanent in both hands, but was ill-defined and transient in the feet. On the second day following operation there was a marked extensor plantar response on the right with fanning of the toes, but this disappeared on the fourth post-operative day. A weak Rossolimo appeared on the right on the second day, and on the left side on the fifth post-operative day. These have increased in magnitude and ease of elicitation, and have remained constant during the two ensuing months , they are still present (April, 1933).

## DISCUSSION AND CONCLUSIONS.

The reflexes which these animals exhibited as a result of the various operative procedures may best be described by stating the phenomena which have been observed after unilateral and bilateral lesions restricted to: Area 4, Area 6, and to Areas 4 and 6 together. It is to be understood that all stated time intervals relate to chimpanzees.

### *Unilateral Lesions.*

(1) *Area* 4.—It has already been pointed out that a lesion sharply restricted to the site of origin of the pyramidal fibres controlling the lower extremity causes a flaccid paralysis with the appearance of a simple unmodified Babinski response, without lateral deviation of the toes. The Chaddock sign is also well developed, and the present observations substantiate those of Schick [20] who found that the Chaddock sign is invariably associated with sign of Babinski in chimpanzees. Tendon reflexes are not exaggerated and the sign of Rossolimo is absent or minimal. Involuntary forced grasping is never seen. The animal recovers its capacity to use the extremity in ordinary locomotor movements quite effectively, but voluntary prehension of the toes is permanently impaired. and may be completely absent for one to two months..

(2) *Area* 6.—Lesions restricted to Area 6 may be followed by a transient positive Babinski response which persists for only a day or two. The fanning sign of Babinski, however, may be present for two to three weeks and sometimes longer, but it may be associated with little or no extension of the toes, and in Experiment 2 fanning was accompanied by an increased *flexor* response of the toes. The Rossolimo phenomenon is always well developed and, while it diminishes with time, was present in one chimpanzee for a period of three months following a unilateral lesion. Finally, the symptoms of involuntary grasping evoked by gentle contact of an object with the sole of the foot is strongly present for a period of two to three weeks and then gradually disappears. The extremities opposite a lesion of Area 6 remain moderately spastic for a period of from one to several weeks.

(3) *Areas* 4 *and* 6.—When both Areas 4 and 6 are removed simultaneously, or in sequence, the Babinski response is very greatly enhanced over that seen following lesions restricted to Area 4, and the fanning sign appears as a second and invariable phase of the Babinski. The sign of Rossolimo is present and becomes exaggerated with other tendon reflexes. As far as we are aware it remains permanently. Forced grasping is also present, and if it had appeared when Area 6 was destroyed before Area 4, it does not immediately disappear when the pyramidal representation in the cortex is destroyed. We are aware that this is contrary to impressions gained from the study of clinical cases.

### *Bilateral Lesions.*

When lesions corresponding to the preceding are made on both sides, the symptoms already present as a result of the unilateral lesions become uniformly and often very dramatically exaggerated on the previously affected, *i.e.*, the ipsilateral, side. Indisputable evidence has been obtained in this way of the existence of bilateral representation in both Areas 4 and 6.

*Area* 4.—When the *motor* representation of the second lower extremity is removed, flaccid paralysis of the contralateral limbs appears, and in addition the symptoms in the previously monoplegic extremity become greatly exaggerated, *i.e.*, motor power is diminished [8, 10], and the Babinski and the Rossolimo signs are increased. Forced grasping and the fan-shaped sign, however, do not appear.

*Area* 6.—Destruction of the second *premotor* area produces in chimpanzees, as Richter and Hines [17, 18] have found in monkeys, the reappearance of the involuntary grasping reflex on the ipsilateral side as well as on the contralateral. In our experience the phenomenon does not become permanent in chimpanzees or monkeys until Area 4 has also been destroyed on both sides. The fanning sign is greatly increased in bilateral preparations restricted to Area 6, but it is also transient. The Rossolimo sign, however, becomes permanent after bilateral premotor lesions.

*Areas* 4 *and* 6.—We have not yet had the opportunity of studying a chimpanzee in which all of Areas 4 and 6 had been destroyed on both sides, but in the chimpanzee "Mussai" (Experiment 4) all of Area 6 and the part of Area 4 corresponding to the entire motor representation of the upper extremity, was destroyed bilaterally. The animal showed grave and permanent impairment of motor performance of the upper extremities with spasticity and very curious restriction of voluntary movement.

In monkeys and baboons in which Areas 4 and 6 have been completely removed bilaterally the animals have suffered virtually complete and permanent loss of voluntary power in all four extremities; forced grasping [3] and spasticity are also permanent and extreme [11] and the involuntary postural and righting reflexes of Magnus and de Kleyn make their appearance [12], From the point of view of its postural reflex status such an animal cannot be distinguished from the thalamic monkeys described by Magnus [15] in which both cerebral hemispheres had been completely removed. It is clear, therefore, that Areas 4 and 6 contain the chief, and probably the only volitionally significant motor projection systems from the cortex.

The preceding observations are summarized in the following table:—

Table I.—Showing Effect on Spasticity and the Pathological Reflexes of Unilateral and Bilateral Lesions of Motor and Premotor Areas in the Chimpanzee.

| | Spasticity | Babinski Chaddock | Toe fanning | Rossolimo and increase of other tendon reflexes | Forced grasping |
|---|---|---|---|---|---|
| Unilateral— | | | | | |
| Area 4 .. .. | Absent | Permanent | Absent | Absent | Absent* |
| Area 6 .. .. | Transient | Absent* | Transient | Permanent | Transient |
| Area 4 and 6 .. | Permanent | Permanent | Transient or Permanent | Permanent | Transient |
| Bilateral— | | | | | |
| Area 4 .. .. | Absent* | Permanent | Absent | Absent | Absent |
| Area 6 .. .. | Transient | Absent* | Permanent | Permanent | Transient |
| Area 4 and 6 .. | Permanent | Permanent | Permanent | Permanent | Permanent |

* Occasionally present for 12 to 48 hours after operation, evidently due to disturbances incident to removal of the area closely adjacent.

From these observations it is clear that the two components of the pathological reflex originally described by Babinski are not produced, in the chimpanzee, by lesions of the same cortical area. Lesions restricted to the origin of the pyramidal tract (Area 4) are invariably followed by a simple extensor toe response without fanning or lateral deviation, but when Area 6 is extirpated also there ensues fanning and lateral deviation of the toes, together with a more pronounced extensor response.

In addition, the excitability of the tendon reflexes becomes markedly exaggerated after lesions of Area 6, but not after lesions restricted to the true motor area. This hyperactivity is accompanied by a Rossolimo response, and by the symptom of involuntary forced grasping which is transient in lesions of Area 6 alone, but becomes permanent when 4 and 6 are extirpated together. The Rossolimo response, however, is peculiarly sensitive and may persist indefinitely after a small unilateral lesion.

When the lesions are of such a nature that the more marked symptoms such as spasticity and forced grasping are transient, *i.e.*, in unilateral lesions of Area 6, the positive Rossolimo response persists after the disappearance of all other pathological signs. Similarly in lesions of Areas 4 and 6 the extensor Babinski response and the Rossolimo sign are permanent and are the most outstanding objective evidence of an abnormal condition in the period after ultimate functional recovery has taken place.

Our observations are borne out by those of Schick alluded to above. He found a Rossolimo response in three infant *Macacus rhesus* monkeys during the first month of life at a time when reflex grasping was prominent. In adult macaques the Rossolimo response cannot be obtained. Goldflam [13] made a similar observation in normal human infants during the first month of life. In studying a large group of diseases of the central nervous system in human subjects, Goldflam also has found the Babinski phenomenon frequently present in the absence of the Rossolimo and *vice versa.* After studying the pathological material in connection with this, he concluded that the Rossolimo reflex is a sign of release of function from a pathway other than the pyramidal tract, but which courses beside it in the lateral columns of the cord.

Since our evidence obtained from anthropoid material is in agreement with that of Goldflam on man that the cortical projection systems responsible for the Rossolimo and for the Babinski extensor phenomena are not the same, a further inference may be drawn that, in human cases of lesions of the cortex, the absence or presence of fanning of the toes, spasticity, and a positive Rossolimo are of value for cortical localization. Presence of a simple extensor Babinski would then be considered as evidence of a lesion restricted to the pyramidal motor system, but a more pronounced extensor response with fanning of the toes and a Rossolimo reflex would suggest a more extensive lesion, involving Area 6 or its projection system from the cortex, which passes through the anterior end of the internal capsule [Poliak 16]. In these circumstances, spasticity would be expected, as well as transient reflex grasping.

It may, therefore, be inferred that the spasticity of a capsular hemiplegia is due to interruption of motor projection systems, from both Areas 4 and 6 (*cf.* Walshe, [21]), and that spasticity is likely to be more pronounced in lesions involving the anterior end of the capsule in addition to the mid-region of the capsule through which the pyramidal fibres pass. Finally, following unilateral lesions, forced grasping and the involuntary postural reflexes of Magnus are transient and become permanent only when the motor projection systems of Areas 4 and 6 from both hemispheres are interrupted [3, 11, 12].

## SUMMARY.

The more common neurological signs have been investigated in tame chimpanzees before and after circumscribed surgical lesions of various excitable regions of the cerebral hemispheres. The excitable cortex of the chimpanzee, as well as of man, consists of two principal areas: (i) the region of origin of the pyramidal pathways (Area 4) which lies just anterior to and within the central sulcus, and (ii) the premotor region (Area 6) lying anterior to Area 4, which, through its connections with the pyramidal tracts and with the basal ganglia, red nucleus and other subcortical regions, serves, as we have pointed out elsewhere [11], to correlate postural with volitional adjustments. Our principal conclusions are as follows:—

(1) Lesions of Area 4 cause *flaccid* paralysis of the contralateral extremities, a Babinski response and diminution of tendon reflexes. These signs become more pronounced after bilateral extirpation of Area 4.

(2) Lesions restricted to the premotor area (Area 6) are followed by *spastic* paresis of the contralateral extremities, together with forced grasping, an increase in tendon reflexes, the Rossolimo response and fanning of the toes. These signs are present for a longer period after

*bilateral* than after *unilateral* lesions of Area 6. Recovery of motor power may be extensive, but the sign of Rossolimo persists permanently, even after a unilateral lesion.

(3) When Areas 4 and 6 are both removed from one cortex, very marked spasticity and forced grasping appear. The extensor Babinski response becomes exaggerated ; Rossolimo's sign is increased and tendon reflexes are permanently exaggerated. Motor deficit, moreover, is permanent and grave.

(4) In all cases of removal of a *second* motor or premotor area, the existence of bilateral innervation has been demonstrated by augmentation of the symptoms in the ipsilateral extremities.

(5) In monkeys and baboons, complete bilateral extirpation of Areas 4 and 6 is followed by permanent and complete loss of voluntary power. Forced grasping and spasticity are extreme, and the involuntary postural and righting reflexes of Magnus and de Kleyn may be demonstrated readily. The bodily reflex status of such animals appears to be identical with that of thalamic preparations.

(6) Presence of spasticity, forced grasping, the fanning sign and the Rossolimo tendon reflex of the digits, thus points to lesions involving the premotor area or its projection system from the cortex, while flaccidity, the simple extensor Babinski response and depression of tendon reflexes, suggests a lesion restricted to the pyramidal tract.

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## NOTICES OF RECENT PUBLICATIONS.

*Anatomie médico-chirurgicale du Système nerveux végétatif.* Par J. DELMAS et G. LAUX. Paris: Masson et Cie. 1933. Pp. 266. Price 80 fr.

In an introduction to this monograph Professor Duval claims as a special merit of it the attempt of the authors to subordinate anatomical description to the conception of an active functioning organ. In this task, the desirability of which is obvious to anyone who reads the numerous textbooks on the autonomic system which have recently appeared, they have largely succeeded; they treat, in other words, the vegetative nervous system as a part of a vital machine and do not merely describe it as seen by the anatomist. The anatomy of its various parts does not, however, suffer from this mode of approach; the relations and connections of the sympathetic ganglia and pathways are clearly but concisely described and illustrated copiously by admirably reproduced plates, as well as by numerous diagrammatic drawings. In their efforts at systematization, as in dealing with the higher centres grouped around the thalamus and third ventricle, they may go beyond definitely established facts, but they are judicious in the use of hypotheses and careful to point out where more evidence is necessary before their views can be definitely accepted. The volume is, unlike many textbooks on the anatomy of the nervous system, obviously based largely on original work and has therefore a personal character which adds to its value. The last section, which is also excellently illustrated, contains descriptions of methods of surgical approach to the more important parts of the vegetative system.

It is admirable both as a textbook and a work of reference, and in the latter respect the bibliography, though it contains mainly French references, will be useful, while if the surgery of this portion of the nervous system ever acquires the importance which the authors tacitly assume it has now, it will be of further service.

*Études neurologiques.* 5me Série. Par G. GUILLAIN. Paris: Masson et Cie. 1932. P. 462. Price 80 fr.

We can extend to the fifth volume of his collected papers the same welcome that we offered to Professor Guillain's earlier volumes. This, as those which preceded it, contains reprints of articles published in various journals or in the records of clinical societies by the chief of the Salpêtrière and his assistants; they are consequently of unequal value, some being merely short notes or clinical descriptions, but others are more elaborate contributions.

As in the previous collections the articles are arranged according to the subjects with which they deal. An index would have made it more useful for the purpose of reference.

*Beiträge zur Kenntnis der Narkolepsie.* Von R. THIELE und H. BERNHARDT. Berlin: S. Karger. 1933. S. 187. Price 18 M.

A series of thirty-five personally observed cases is described, together with the records of seriological and radiographic investigations.

The clinical picture of narcolepsy as observed by the authors and described in the literature is summarized and discussed. There is a lengthy and speculative chapter on ætiology and pathogenesis from which no new facts emerge. By way of treatment the use of ephedrin is recommended as sometimes of value in reducing the frequency of the attacks of sleep, though the authors have found it ineffective in the case of cataplexy.

*Hirn und Ohr.* von K. GRAHE. Leipzig: G. Thieme. 1932. S. 108. Price 9.60 M.

The accurate examination of hearing and of the functions of the vestibular apparatus has not as a rule received in neurology the attention it deserves. This small book is timely as it shows what information may be sometimes obtained by such investigations, and as in it the author describes concisely and clearly the methods of making them. It is the chapter on the methods of examination which will be of most value to the neurologist, for by a study of it he can easily learn to carry them out himself and not refer his patients for this purpose to an otologist, a common but not very satisfactory arrangement.

The description of the disturbances of these functions by various peripheral and central lesions shows what information may be obtained, but the conclusions drawn from them need critical evaluation from the neurological point of view.

*Moderne Therapie der Neurosyphilis.* von B. DATTNER. Wien: W. Maudrich. 1933. S. 334. Price 22 M.

The earlier chapters of this volume describe in detail the pathological investigations necessary for the diagnosis of neurosyphilis, as the examination of the cerebrospinal fluid, and discuss fully their value and significance. The greater part of it is, however, devoted to questions of treatment, the general principles being first discussed and later the treatment of the more important diseases, as dementia paralytica and tabes. The reader will be introduced to many drugs scarcely known in this country, and, as might be expected of an author of the Vienna school, great emphasis is also laid on fever-producing methods, as infection by malaria, recurrent fever and rat-bite fever. This monograph is an exceptionally important contribution to the subject with which it deals.

*Alcohol and Man. The Effects of Alcohol on Man in Health and Disease.* Edited by H. EMERSON, etc. New York: The Macmillan Co. 1932. Pp. 451. Price 18s.

The age-long discussion on the effects of alcohol on man is taken up here again by a group of writers, clinical, physiological, pharmacological, psychiatric, statistical and others, each of whom is responsible for a separate section in which he expresses his views based on his own work and experience. Every part of the subject is adequately covered, and though each author is writing independently of the others the various chapters are so well edited and arranged that as a whole the book is easily read, while, on the other hand, any part of the subject may be readily referred to in it. The aim of the editor has been to present to the educated layman such facts and opinions on the influence of alcohol in either moderate or excessive amounts as appear sufficiently established from the social and biological as well as from the medical point of view. He has succeeded in producing a volume which can be recommended to all interested in this important subject.

*An Introduction to Analytical Psychotherapy.* By T. A. ROSS. London: Edward Arnold. 1932. Pp. 203. Price 10s. 6d.

This book rests on a wide experience, and is honest, clear and reasoned. But it is written so sensibly, its author has so wisely refrained from extravagant or over-subtle interpretations, that one is apt to ignore the intellectually unsatisfying nature of the moderate theory put forward and its implications, if logically pursued. This is, however, no defect, since the pragmatic test is decisive in psychotherapy, if anywhere; and it is well known that the author of this work is a most successful psychotherapist. As Prinzhorn and many others have pointed out, there is a wide gulf between the methods efficacious in mental healing and those of medicine generally, the personality of the physician and his relationship to the patient being decisive in the former, while his theory and mode of procedure are of minor importance. As the brevity of the chapter on technique shows, practical psychotherapy cannot be set down in a scheme or taught; it must be learnt by personal experience in one's work with patients, and to those who wish for guidance in this empirical training Dr. Ross's book will prove of value.

*Éther, Cocaine, Hachich, Peyotl et Démence précoce. Essai d'Exploration pharmacodynamique du Psychisme des Déments précoces.* Par ANDRÉE DESCHAMPS. Paris: Les Éditions Vega. 1932. Pp. 210.

The influence of drugs such as amytal and carbon monoxide on catatonic states has received much attention in the last few years, as has also the study of abnormal states produced in healthy people by mescalin, hashish, etc. The author of this monograph, prompted and directed by his teacher C. Pascal, has given to thirty-two patients with gross schizophrenic features ether, cocaine, caffeine and hashish, either alone or, as in most cases, combined: two patients were given peyotl. Improvement in the drugged state was found in the cases with a better prognosis. Where a previously mute patient spoke while under the influence of the drugs, his thought seemed to show features distinct from what is found in toxic states or in archaic modes of thinking. Therapeutic applications of the method are suggested and numerous points in psychopathology are dealt with. As a whole the monograph has an amateurish stamp; the examination of the evidence is rather superficial and uncritical, but there is much of interest in the research.

*Naturgeschichte der Seele und Ihres Bewusstwerdens: Mnemistische Biopsychologie.* von EUGEN BLEULER. Zweite Auflage. Berlin: Springer. 1932. Pp. 268. Price Rm. 16.

This second edition of Professor Bleuler's book may be set alongside the last production of another distinguished Swiss, von Monakow, as an ordered attempt to sum up human psychology from a biological point of view. The method used is that of the natural sciences; and the too-familiar insistence on the alleged conceptual necessity for a cleavage between physical and psychical is repudiated. The presentation of this way of regarding human activity is slightly modified from that of the first edition, especially in regard to consciousness and perception. In an energetic foreword Bleuler examines and rejects some criticisms which came chiefly from philosophers. The body of the work deals with the derivation of consciousness from the integrated function of the central nervous system and with the apparatus of the mind. This erudite and complicated design for a mnemistic psychology is a notable contribution towards the understanding of the relation between mental functions and the total activity of the central nervous system.

*Allgemeine Neurosenlehre auf psychoanalytischer Grundlage.* von HERMANN NUNBERG. Bern: Huber. 1932. Pp. 339. Price Sv. Fr. 15.

There have hitherto been available only two fairly comprehensive and adequate formulations of the body of psycho-analytic doctrine, Freud's "Introductory Lectures" and the non-committal Healy-Bronner-Bowers volume. The present work may be accepted as an authoritative and better-organized account of the opinions now held in the Viennese stronghold of psycho-analysis; Freud, in his brief preface, calls the book "the most complete and conscientious presentation of a psycho-analytic theory of neurotic processes that we have." Such an imprimatur makes the book valuable in a field so much at the mercy of dogmatism and wordy speculation; one can here examine the theory and method of psycho-analysis as acknowledged by its founder. At some points there is considerable divergence from the views now current in the English school, but this may not be a disadvantage. The book is coherent and well arranged, but there is much repetition. On the whole, where it is difficult to read this is due not so much to its style as to its subject and mode of thought. It is noteworthy that in a book of 312 pages, only 19 are specifically devoted to the theoretical basis of therapy.

*Human Values in Psychological Medicine.* By C. P. BLACKER, London: Oxford University Press. Humphrey Milford. 1933. Pp. 179.

Philosophical speculations about psychology and mental disorder are usually jejune and often ill-informed; but to this book, written by an experienced psychiatrist, no such objection can be made. It is, on the contrary, stimulating and sound. The author has applied to his clinical material a general theory in which human idiosyncrasy, the groundwork of medical psychology, is regarded as lying mainly in the realm of affective life and expressing itself in the individual's values. The biological implications and development of the author's views are set forth with especial vigour in the valuable chapter on life and death instincts, in which the Freudian teachings on the subject are discussed. In the body of the book the phenomena of mental life, both normal and morbid, are reviewed in the light of the general theory, and an interpretation of them offered which has the merit of lucidity, cohesion and a just biological foundation.

*Das Rechtsgefühl.* von A. E. HOCHE. Berlin: Springer. 1932. Pp. 102. Price Rm. 5.80.

This small book embodies the views of one of the most distinguished of German psychiatrists of the last generation who has latterly occupied himself chiefly with the forensic and social bearings of his subject. He here discusses the psychology of social justice, of the feelings on which equity and right are based for the individual. The psychiatric significance of this is seen in paranoid states and in certain forms of psychopathic personality. The author, however, enlarges his theme to cover questions of politics: the book is informed by a conception of human rights to which the recent developments in Germany are an ironical commentary. The book is written with great clearness of thought and diction, and is an interesting contribution to social psychology.

*Emigration and Insanity.* By ÖRNULV ÖDEGAARD. Copenhagen: Levin and Munksgaard. 1932. Pp. 206.

The study of racial psychiatry is a difficult field in which linguistic and cultural obstacles or political prejudices make the observations of most writers as questionable as their conclusions. Dr. Odegaard's investigation, however, is a model of what such a study should be. He has compared the incidence of mental disorder in the Norwegian-born population of Minnesota with that in Norway and has considered the relevant social problems. He finds that exogenous factors are more significant in the psychoses of immigrants than constitutional ones, and he accounts for the relative frequency of schizophrenia among them by supposing that a schizoid personality predisposes to restlessness and so to emigration. The strain of immigrant life does not seem to have played a part in the causation of the endogenous psychoses. The work is presented clearly, though in considerable detail, and is of anthropological, as well as psychiatric, importance.

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EDITOR.

Book No.........

SEPTEMBER, 1933.

BRAIN.

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# THE CLINICAL SIGNIFICANCE OF THE ANTERIOR CHOROIDAL ARTERY.

BY A. A. ABBIE, M.B., B.S., B.SC. (SYDNEY).[1]
(*Institute of Anatomy, University College, London.*)

THE clinical importance of the anterior choroidal artery is still strangely neglected, despite the attention devoted to this subject by Continental workers. Consequently, a short description of the morphology of this vessel, and an account of its distribution in man, are not out of place at a time when attention is being redirected towards the study of cerebral arterial supply generally.

Heubner, in 1874 [1], showed that the anterior choroidal artery supplied part of the posterior limb of the internal capsule, and Kolisko, in 1891 [2], gave a good description of its field of supply. In 1905, von Monakow [3] showed that he was aware that the anterior choroidal artery supplied part of the lateral geniculate body, and in 1909 Beevor [4], in his classical work, described fairly completely the whole field of distribution of this vessel. More recently, Mme. Schiff-Wertheimer [5] and Ley [6] have paid some attention to the anterior choroidal artery and have described cases wherein it has been affected. The comparative aspect of the problem has been studied by Hofmann [7] and Bertha de Vriese [8], but it is clear that neither had realized its full significance.

Neither the complete area of its distribution nor the full story of its phylogeny has so far been described; these will be discussed more fully elsewhere, but a brief summary of the phylogenetic story will be useful here since it is to phylogeny that we must look for explanation of variations.

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[1] "Walter and Eliza Hall" Travelling Medical Research Fellow of Sydney University.

## MATERIAL AND METHODS.

The anterior choroidal artery has been dissected in sixteen human hemispheres, and in a phylogenetic series of brains, including amphibia, *Sphenodon*, crocodiles, marsupials, sheep, lemurs and monkeys. In addition, its mode of origin was studied in eighty human hemispheres.

The artery was injected in most cases with indian ink by means of a hypodermic syringe and fine needle; the terminal branches were then followed individually to their ultimate distribution. In all cases the findings were checked against horizontal and coronal sections of similar brains to ensure accuracy of localization.

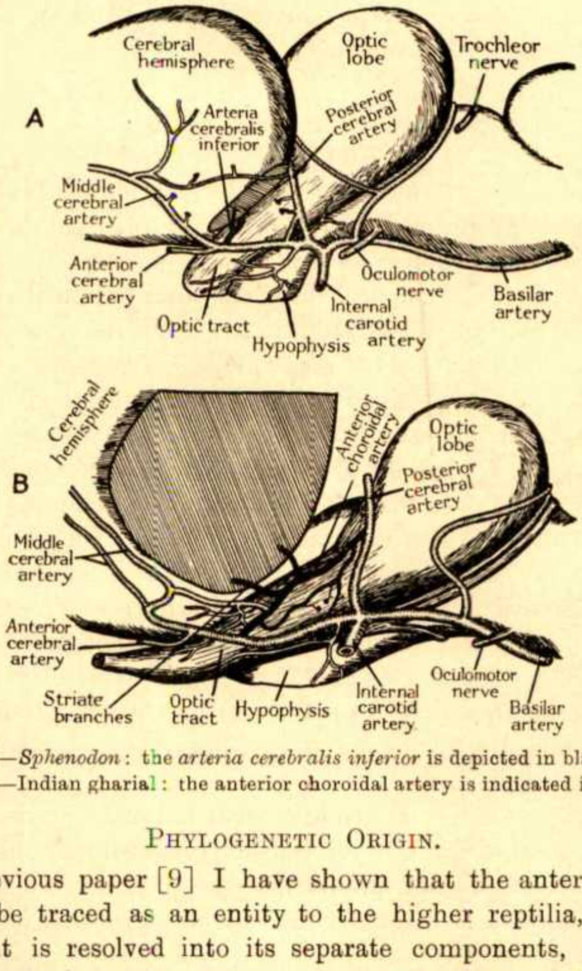

FIG. 1 A.—*Sphenodon*: the *arteria cerebralis inferior* is depicted in black.
FIG. 1 B.—Indian gharial: the anterior choroidal artery is indicated in black.

## PHYLOGENETIC ORIGIN.

In a previous paper [9] I have shown that the anterior choroidal artery can be traced as an entity to the higher reptilia, but that in *Sphenodon* it is resolved into its separate components, each with a distinctive field of supply. These components (fig. 1A) are, on the one hand, the inferior cerebral artery of Dendy [10] arising from the cranial division of the internal carotid artery; on the other, a series of branches from the posterior cerebral artery. The inferior cerebral artery in amphibia and *Sphenodon* is distributed to the palæostriatum and the pyriform cortex, the posterior cerebral contributions supply the optic tract, lateral geniculate body and cerebral peduncle. In amphibia the inferior cerebral artery is often represented by a series of small vessels instead of by a single larger trunk.

In the crocodile the inferior cerebral artery has joined the posterior cerebral contributions to form a continuous vessel or network of tiny vessels arising from the cranial artery, running posteriorly and dorsally along the optic tract and diencephalon and joining the posterior cerebral artery (fig. 1B). At this stage of evolution the anterior choroidal artery plays no part in the supply of the choroid plexus of the telencephalon; this supply is still entirely from the posterior cerebral artery.

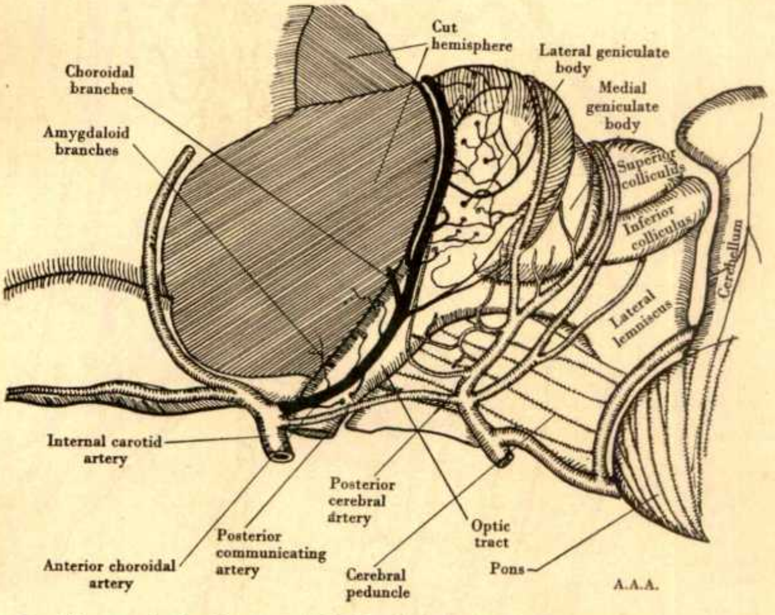

FIG. 2.—The arteries in the marsupial (Dendrolagus): the anterior choroidal artery is injected with indian ink.

In marsupials and true mammalia the cerebral hemispheres have so enlarged that they have acquired an inferior horn to the lateral ventricle; the choroid plexus has become elongated and lies alongside the optic tract. Now the anterior choroidal artery takes over from the posterior cerebral artery some of the choroidal supply and becomes a true choroidal artery. This vessel arises from the cranial division of the internal carotid artery, before the origin of the middle cerebral artery, and runs posteriorly and dorsally along the optic tract and diencephalon to terminate in the posterior cerebral artery (fig. 2). On its way it supplies part of the pyriform cortex and underlying amygdaloid nucleus, part of the corpus striatum, the optic tract and part of the lateral geniculate body, part of the cerebral peduncle and subthalamic region, part of the internal capsule and the antero-inferior part of the choroid plexus. The beginning of the caudal division of the internal carotid artery is represented by the posterior communicating artery; the posterior cerebral artery is so strongly connected with the basilar as to

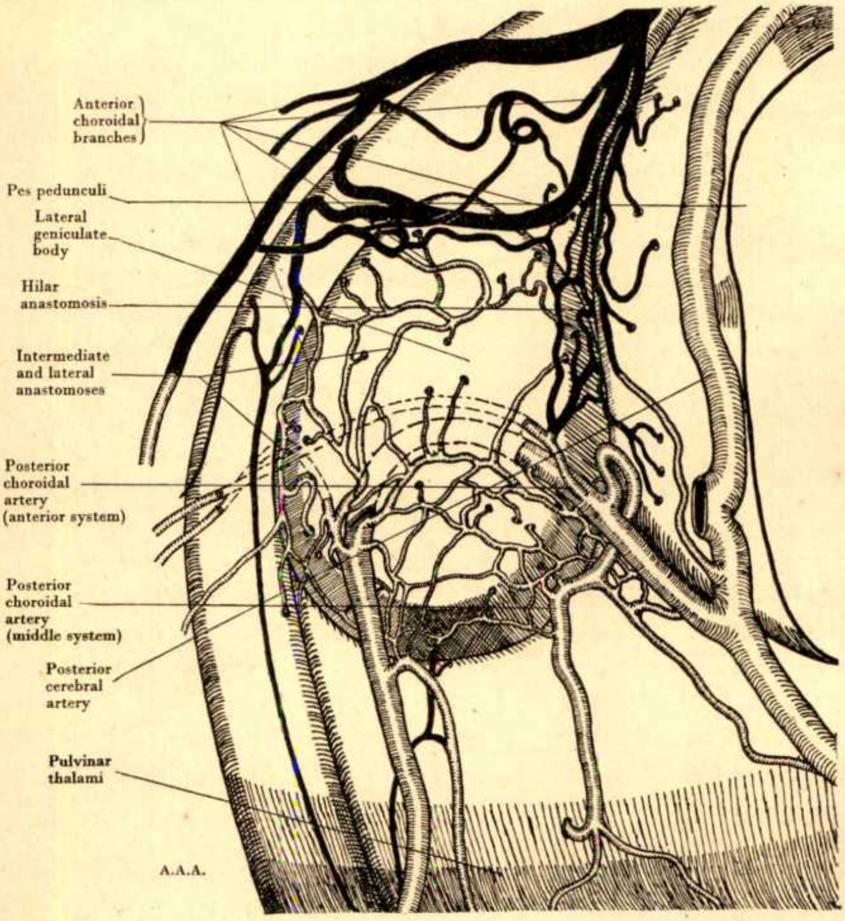
Anterior choroidal branches
Pes pedunculi
Lateral geniculate body
Hilar anastomosis
Intermediate and lateral anastomoses
Posterior choroidal artery (anterior system)
Posterior choroidal artery (middle system)
Posterior cerebral artery
Pulvinar thalami
A.A.A.

FIG. 3.—Human: dissection to show the termination of the anterior choroidal artery (black) in the posterior cerebral. The injection has not entered all the finer branches.

give the impression that it arises from this and not from the internal carotid artery.

Subsequent change is of degree only: with the increasing size of the cerebral hemispheres and consequent enlargement of the inferior horn of the lateral ventricle and its choroid plexus, the choroidal contributions from the anterior choroidal artery increase progressively in importance. In the sheep these choroidal branches are few and small; in the monkey they equal in size the branches by which the anterior choroidal artery terminates in the posterior cerebral; in man they appear to form the main channel of the artery, the termination of this in the posterior cerebral branches being small and often hard to find (fig. 3). Intermediate conditions are, however, frequently seen in human brains.

The foregoing description covers briefly the evolution of the anterior choroidal artery and provides clues for the solution of the problem of its variation. It will be better, however, to defer discussion of variation until the normal distribution in man has been described.

## Distribution in Man.

In man a standard of normality for the anterior choroidal artery has been set; this gives a fairly accurate description of its usual mode of origin and maximum area of distribution. The artery arises from the stem of the internal carotid artery between the points of origin of the posterior communicating and middle cerebral arteries. Thence it crosses the optic tract from the lateral to the medial side and runs posteriorly along the medial border of the tract against the cerebral peduncle. At the anterior pole of the lateral geniculate body it divides into many branches, most of which recross the optic tract to enter the inferior horn of the lateral ventricle and reach the choroid plexus. The true terminal branches, however, run posteriorly over the lateral geniculate body to join the posterior cerebral and posterior choroidal arteries (fig. 4).

The branches of the anterior choroidal artery arise in series along its length, and proceed in order to their destinations. Close to the origin arise branches which supply part of the head of the caudate nucleus and the postero-medial border of the anterior commissure. Next, some vessels reach the pyriform cortex and uncus and supply the postero-medial part of the underlying amygdaloid nucleus; similar vessels are distributed to the antero-inferior part of the hippocampus and fascia dentata and the cauda fasciæ dentatæ. The branches to the pyriform cortex anastomose with branches from the middle and posterior cerebral arteries; those to the uncus and fascia dentata with branches of the posterior cerebral artery.

More posteriorly a series of branches pierces the optic tract; these play little part in the supply of the tract, but pass dorsally into the base of the brain to reach the posterior two-thirds of the posterior limb of the internal capsule (which they supply to the level of the upper border of the middle segment of the lenticular nucleus); the medial segment and medial part of the middle segment of the lenticular nucleus (that is, most of the globus pallidus); and the beginning of the optic and, probably, acoustic radiations as far laterally as the lateral wall of the descending horn of the lateral ventricle (fig. 5). The arteries of supply to the optic tract pass medially and dorsally between the tract and the peduncle, they then turn laterally to enter the dorso-medial aspect of

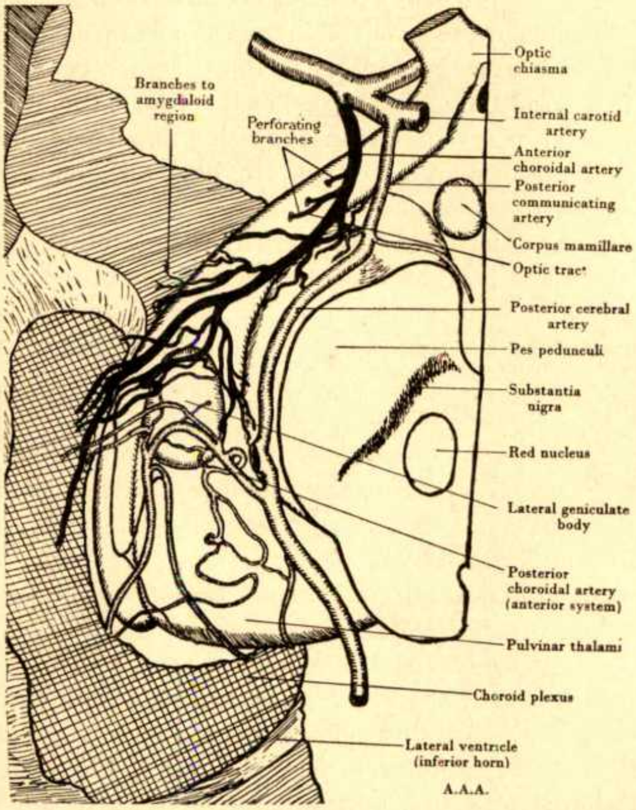
Branches to amygdaloid region
Perforating branches
Optic chiasma
Internal carotid artery
Anterior choroidal artery
Posterior communicating artery
Corpus mamillare
Optic tract
Posterior cerebral artery
Pes pedunculi
Substantia nigra
Red nucleus
Lateral geniculate body
Posterior choroidal artery (anterior system)
Pulvinar thalami
Choroid plexus
Lateral ventricle (inferior horn)
A.A.A.

FIG. 4.—Human: dissection to show the general course and relations of the anterior choroidal artery.

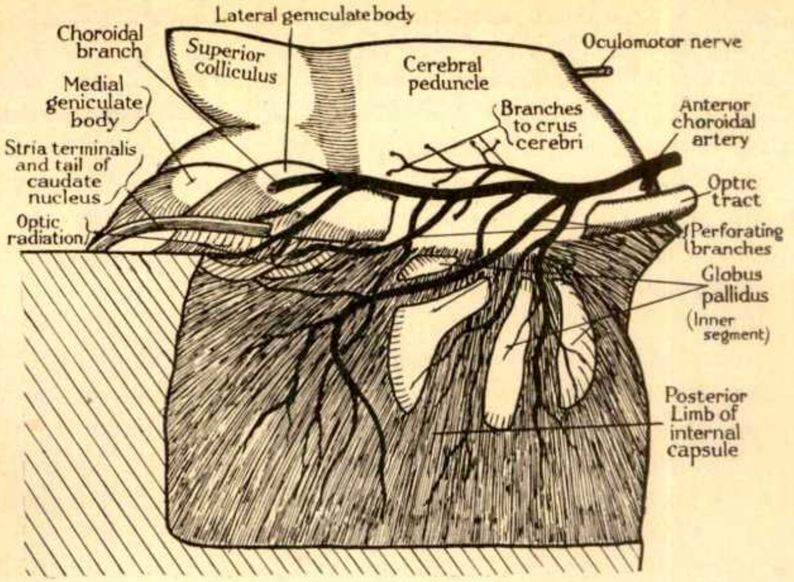

Fig. 5.—Human: dissection to show the distribution of the anterior choroidal artery to the posterior limb of the internal capsule, globus pallidus, optic radiation and stria terminalis.

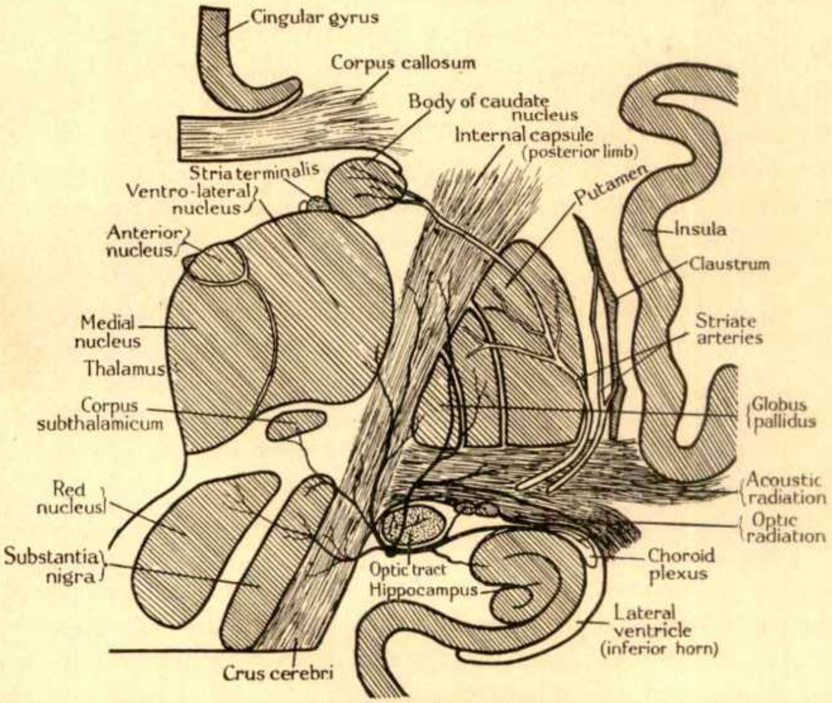

Fig. 6.—Human: semi-schematic, illustrating the distribution of the anterior choroidal artery to the crus cerebri, substantia nigra, red nucleus, corpus subthalamicum, ventro-lateral nucleus of the thalamus, posterior limb of the internal capsule, globus pallidus, optic radiation, optic tract, stria terminalis and tail of caudate nucleus, fascia dentata and choroid plexus.

the tract. In sub-primates the vessels of supply to the optic tract enter its superficial surface and it is reasonable to suppose that this rotation medially in primates is associated with the eversion of the dorsal nucleus of the lateral geniculate body as described by Brouwer and Zeeman [11]. The branches to the optic tract anastomose freely in the pia mater with branches from the posterior communicating artery with which there is considerable overlap, and, but to a lesser extent, with twigs from the middle cerebral artery.

Branches from the anterior choroidal artery reach the cerebral peduncle where they anastomose with branches from the posterior communicating and posterior cerebral arteries. The middle third of the crus which contains the descending motor fibres is, however, constantly supplied by the anterior choroidal artery, some of whose branches pass right through to reach the upper part of the substantia nigra and red nucleus, the corpus subthalamicum and, frequently, the most superficial part of the ventro-lateral nucleus of the thalamus (fig. 6).

From the main trunk or, more frequently, from one of its terminal divisions, arises a constant vessel which enters the stria terminalis and the tail of the caudate nucleus and runs posteriorly and dorsally in these to the level of junction of the body and descending horn of the lateral ventricle; this artery supplies both structures to this extent. The arterial supply to the lateral geniculate body has been fully described in my previous paper; briefly, the anterior choroidal artery supplies the lateral, and the posterior cerebral artery the medial aspect of this body; the intervening hilar region is supplied by both. The branches to the choroid plexus are numerous and large; they enter the antero-inferior part of the plexus and break up into a large number of small twigs, some of which supply the walls of the ventricle, the remainder anastomose freely with posterior choroidal branches. Under favourable circumstances a large anterior choroidal branch can be traced posteriorly and dorsally along the medial border of the plexus to the foramen of Monro, but it is rarely possible to inject it in its full extent.

## VARIATIONS.

In a discussion of the possible variations of the anterior choroidal artery it is necessary to appreciate fully the implications of its double origin. We have seen that the vessel consists essentially of two parts: one, arising from the cranial division of the internal carotid artery to supply the palæostriatum and pyriform cortex, the other taking origin from the caudal division and supplying the remainder of the anterior choroidal field; the former may be considered to have cranial affinity, the latter caudal. We have also seen that either component may be represented in part or entirely by a series of small vessels which subserve its final distribution; thus we have an anatomical foundation for a discussion of variation.

The cranial component is mainly palæostriatal in distribution and supplies, in addition to the pyriform cortex, part of the head and most of the tail of the caudate nucleus, the postero-medial part of the amygdaloid nucleus and most of the globus pallidus. Variations will be expressed by mode of origin of its branches but, however they arise, they must do so from the cranial division of the internal carotid artery. That is what occurs: one of the most frequent variations is the independent origin from the stem of the internal carotid, or from the middle cerebral artery, of any or all of the branches to the caudate and amygdaloid nuclei and to the uncus. The anterior choroidal artery itself may, very rarely, arise from the middle cerebral artery.

The caudal component supplies the optic tract and lateral part of the lateral geniculate body, the middle third of the crus and the subthalamic region, the posterior two-thirds of the posterior limb of the internal capsule and the optic radiation, the antero-inferior parts of the fascia dentata, hippocampus and choroid plexus. In this case we should expect variations of supply to be with posterior cerebral branches, and that is what is found: the posterior communicating artery may be enlarged at the expense of the anterior choroidal and take over some of its field of supply; on the other hand the anterior choroidal artery may predominate. Rarely, the posterior communicating is absent; then the first part of the posterior cerebral artery may follow the course, and distribute the branches of the anterior choroidal; this is especially obvious when the communication between the basilar and posterior cerebral arteries is small. Again, as Kolisko has observed, the branch which usually arises from the posterior communicating artery to supply the genu and anterior third of the posterior limb of the internal capsule may come from the anterior choroidal artery when this is enlarged; on the other hand, when the anterior choroidal artery is smaller than usual the posterior communicating artery supplies a greater proportion of the posterior limb of the internal capsule. Similarly, the substantia nigra, red nucleus and corpus subthalamicum may receive their blood from the posterior cerebral artery; or the posterior communicating artery play a larger part than usual in the supply of the optic tract.

These are all examples of the interchangeability of the origins of arteries, but it will be noted that this variation is not haphazard, it occurs only among vessels which have a common phylogenetic origin. In the examples just discussed the arteries may be considered as being cranial or caudal equivalents, they do not arise indifferently from either component but take origin in an orderly manner from their own parent stock. Such variations do not diminish our faith in arterial constancy, rather do they strengthen our belief in this principle. The anomalous results obtained by Beevor and others who have worked in this field must be attributed to their failure to recognize the importance of the phylogenetic history of the cerebral arteries.

Hofmann was so impressed by the caudal affinities of the anterior choroidal artery that he included it in his series of posterior cerebral arteries as the *arteria cerebralis posterior a.* Schiff-Wertheimer regarded the anterior choroidal artery as having two methods of distribution: a terminal to the internal capsule and optic tract, and a double (due to overlapping of supply with the carotid, middle cerebral, posterior communicating and posterior cerebral arteries) to the remainder of the field of supply. This principle is correct and important but, to make it complete, we must add to the terminal field the optic radiation, middle third of the crus, most of the globus pallidus and the lateral part of the lateral geniculate body. Now we can say that the anterior choroidal artery probably always supplies part of the optic tract and the lateral part of the lateral geniculate body, the posterior two-thirds of the posterior limb of the internal capsule, most of the globus pallidus, the optic radiation and the middle third of the crus; it *may* supply part of the head of the caudate nucleus, the pyriform cortex, the uncus and postero-medial part of the amygdaloid nucleus, the substantia nigra, red nucleus, corpus subthalamicum and superficial aspect of the ventro-lateral nucleus of the thalamus.

When we assess the relative clinical values of the two methods of distribution, we see at once that the terminal field of supply—which is practically constant—is also the most important. In diagnosis we are restricted to lesions of those regions which produce definite symptoms and observable signs; the crus, lateral geniculate body, posterior limb of the internal capsule and the optic radiation are such; the head of the caudate nucleus, the amygdaloid nucleus and the subthalamic region are not. Thus we come to the conclusion that the regions most affected by variation of the anterior choroidal artery are least important clinically; those least affected by variation have the greatest clinical importance. Therefore, no percentage list of variations is given; it would not assist diagnosis, nor, even if accurate, would it enable us to forecast the arrangement of the cerebral arteries in any patient before autopsy; at best we could only guess. It is fortunate, then, that lesions of the anterior choroidal artery nearly always cause damage to such structures as produce definitely observable effects, and that the symptom complex is so constant.

## CLINICAL SIGNIFICANCE.

In dealing with lesions of the anterior choroidal artery we are restricted to obstructive conditions causing necrosis in a circumscribed area. Hæmorrhages into the posterior limb of the internal capsule are common enough, but although it is felt that many of these have been attributed erroneously to other than the anterior choroidal artery, the consequent destruction is usually so extensive as to render identification of the vessel involved difficult or impossible.

Proved cases of occlusion of the anterior choroidal artery are rare—a fact commented upon by most writers on this subject; Kolisko has recorded two, Schiff-Wertheimer one, Ley one, and one case has been communicated to me by Dr. Ivy Mackenzie of Glasgow; in the last, both arteries were affected. A search of the available literature has revealed no others; even the large series collected by Henschen [12] contains none attributed by him to lesion of the anterior choroidal artery. Consideration of some ot his clinical and pathological findings, however, leaves no doubt that they were due to involvement of this vessel, but there is no description of the arteries to prove this.

For clinical signs and symptoms of lesion of the anterior choroidal artery we must look to the terminal field of distribution of this vessel: to the posterior limb of the internal capsule in its posterior two-thirds, the beginning of the optic radiation, the middle third of the crus cerebri and the lateral part of the lateral geniculate body; involvement of the globus pallidus causes no effects of clinical value and necrosis of the optic tract, even when present, is very restricted and appears to cause little interference with sight. The characteristic syndrome, then, depends upon destruction in these regions and, as may be expected, comprises hemiplegia, hemianæsthesia and hemianopia, all towards the side opposite to the lesion. These will be considered very briefly in order.

Hemiplegia is constant; it is recorded in all cases. In one of Kolisko's cases clinical details are wanting, but the destruction found in the posterior limb of the internal capsule at autopsy leaves no doubt that the pyramidal fibres were destroyed. In the case recorded by Dr. McKenzie both anterior choroidal arteries were affected, but the hemiplegia and hemianæsthesia were confined to the right side of the body. Facial paresis is recorded by Kolisko and Dr. McKenzie and is suggested by Ley; in Kolisko's case the anterior half of the posterior limb of the internal capsule was unaffected, nor is this usually supplied by the anterior choroidal artery; we must conclude, then, that the crus had undergone some destruction, although such is not recorded. In Dr. McKenzie's case the examination of the brain is not yet complete, but there was definite degeneration of the middle third of the crus; in Ley's case there was destruction in both the posterior limb of the internal capsule and the crus.

Hemianæsthesia, again, is recorded in all cases; it is usually incomplete, but involves all forms of sensation. Hemianopia is recorded by Schiff-Wertheimer and Ley, but not by Kolisko. Schiff-Wertheimer and Ley both describe the hemianopia as complete and towards the right; in the one case recorded by Kolisko in which clinical findings are available there is the specific denial of any interference with vision. In Dr. McKenzie's case hemianopia was not complete; the visual defect comprised a bilateral homonymous superior quadrantic hemianopia so that nearly the whole of the upper field of vision was lost, but the macular field was mostly spared. This has been correlated in my previous paper with the degeneration found in the lateral parts of both lateral geniculate bodies, corresponding with the field of supply of the two anterior choroidal arteries and with the retinal projection areas described by Brouwer and Zeeman. There was, in addition, some loss of the lower right nasal field of vision, resulting, probably, from the degeneration found in the optic radiation. The type of visual defect following occlusion of the anterior choroidal artery appears to depend upon the site of obstruction; it is possible, for instance, for the branches to the lateral geniculate body to be affected and those to the radiation to escape; also, since at least two vessels usually pass to the optic radiation, it is possible for one of these to be obstructed and not the other, so that part of the radiation would escape destruction and the hemianopia be incomplete. Further, the branches to the internal capsule may be involved and those to the visual apparatus escape entirely: upon some such facts must depend the recorded variation of visual defect. The very circumscribed areas of necrosis found in the optic tract in some cases appear to have little effect upon vision.

## POST-MORTEM FINDINGS.

Pathological records are available in the cases described by Kolisko (both cases) and Ley; Schiff-Wertheimer gives none and those of Dr. McKenzie's case are not yet complete. In the cases of Kolisko and Ley degeneration was found in the posterior limb of the internal capsule, restricted by Kolisko to the posterior half; Schiff-Wertheimer states that all the posterior limb except the genu and surrounding parts may be involved. Destruction of the greater part of the globus pallidus appears to be constant, also of part, at least, of the retro-lenticular part of the internal capsule and of the optic radiation. Ley and McKenzie record degeneration in the cerebral peduncle and Schiff-Wertheimer states that this occurs. Degeneration of the lateral aspect of the lateral geniculate body was found by McKenzie and is recognized by Schiff-Wertheimer; degeneration in the optic tract is also recognized by her. In addition, degeneration in the head of the caudate nucleus is described by Kolisko, Ley and Schiff-Wertheimer; in the anterior commissure by Kolisko and in the amygdaloid nucleus by Schiff-Wertheimer. The pathological findings, then, correspond very closely with both anatomical and clinical investigation.

## SUMMARY.

(1) The anterior choroidal artery has two component parts: the cranial is distributed to the pyriform cortex and palæostriatum, the caudal to the remainder of the field of supply.

(2) Variations can be expressed in terms of this double field of supply: the two major vessels may take over more or less of the area of distribution of the two components.

(3) In man, the artery has a constant terminal field of supply which comprises the posterior two-thirds of the posterior limb of the internal capsule, most of the globus pallidus, the beginning of the optic radiation, the lateral aspect of the lateral geniculate body and the middle third of the crus cerebri; the rest of the field is of a double nature, being overlapped by branches of the cranial and caudal arteries.

(4) Variations are common but chiefly affect the double field of supply which is unimportant clinically. The field of major clinical importance is the terminal area of distribution, which is least affected by variation.

(5) Complete occlusion of the anterior choroidal artery presents a constant clinical picture because of the constancy of supply to the

terminal field. Occlusion of individual branches will give a variety of signs and symptoms depending upon the particular branches involved.

(6) The usual clinical picture comprises hemiplegia, hemianæsthesia and hemianopia, all towards the opposite side from the lesion. Of these, hemiplegia is most constant, hemianopia most liable to variation.

(7) Of the five clinical cases recorded, four are lesions of the left anterior choroidal artery, the other is bilateral.

## ACKNOWLEDGMENTS.

I have to express my gratitude to Prof. Elliot Smith who placed at my disposal the bulk of the material used. Dr. McMaster and Dr. Una Fielding of the same department have kindly lent the *Sphenodon* and marsupial material respectively, and to Dr. Fielding I am indebted for helpful advice and criticism. Prof. Shellshear of Hong Kong aided me from his great store of cerebral arterial knowledge. Finally, my thanks are due to Dr. Ivy McKenzie for valuable clinical data and pathological material.

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# CYSTIC OLIGODENDROGLIOMAS OF THE CEREBRAL HEMISPHERES AND VENTRICULAR OLIGODENDROGLIOMAS.

BY J. GODWIN GREENFIELD
AND
E. GRAEME ROBERTSON.
*(From the National Hospital for Nervous Diseases, Queen Square, London.)*

In 1926 Bailey and Cushing first described under the name "oligodendroglioma" a rare form of tumour of the cerebral hemispheres. The slow rate of growth of these tumours, the presence in them of granules opaque to X-rays, and the narrowness of the zone of delimitation between tumour and brain tissue made them particularly favourable for surgical removal.

In 1929 Bailey and Bucy gave a more complete pathological description of these tumours, proving that the majority of the cells of which they were composed were oligodendrocytes, although astrocytes and transitional forms between these and oligodendroglia were also present. Two of the four tumours described in their paper were cystic, one containing 30 c.c. of fluid and the other showing several small cysts on section.

Subsequent papers by Martin and by Roussy and Oberling have confirmed the description given by Bailey and Bucy, but have added several points of interest. Martin showed that the length of history depended to some extent on the position of the tumour, since those near the midline, by obstructing the cerebrospinal fluid pathways, tended to bring on symptoms of increased intracranial pressure at an earlier stage than those situated more laterally in the hemispheres. He also showed that when oligodendrogliomas reach the ventricles they may grow diffusely along their walls, eventually reaching the iter of Sylvius and the fourth ventricle.

Roussy and Oberling are inclined to group with the oligodendrogliomas the tumours which Bailey and Cushing called polar spongioblastomas; otherwise their description of the tumours agrees with that of Bailey and Bucy. Both insist on the presence of mucinoid degenerative changes in the tumour cells by which either the cell body or the intercellular substance becomes stainable by muci-carmine.

Further experience of these tumours has shown that they are not always as innocent and slowly growing as the original description suggested. Abundant mitoses and metastases into the scalp have been described by Martin and by Bailey and Bucy. On the other hand the presence of a few mitoses does not necessarily indicate malignancy, as Bailey and Bucy described a case with this type of tumour in which life was prolonged for more than eight years after the first operation.

Our experience agrees with that of Bailey and Cushing on the rarity of these tumours. We have found nine cerebral oligodendrogliomas in a series of 230 cerebral gliomas which have been examined since the publication of their monograph. If we accept only the classified gliomas in their series, their figures, nine oligodendrogliomas among 254 gliomas, are almost identical. Roussy and Oberling have found them more frequently than this, as they speak of 16 oligodendrogliomas in a series of 251 cerebral tumours.

In the present communication we wish to draw attention to the alterations from the typical clinical and pathological pictures which may take place when oligodendrogliomas of the cerebral hemispheres become cystic and when they grow primarily in the ventricles. A record of five cases of this kind may be of value in supplementing the classical description given by Bailey and Bucy.

*Case* 1.—A. R., a woman, aged 61, was admitted to the National Hospital, Queen Square, under Dr. Riddoch in November, 1931. She had suffered since March, 1931, from headache, vomiting and loss of sense of smell. Two months after the onset of symptoms papillœdema was found in the right eye only. In September bilateral papillœdema and a bitemporal hemianopia were found at the Birmingham General Hospital and operation was advised, but was refused by the patient. There had been a marked failure of memory and slowing of all intellectual processes. On admission there was bilateral papillœdema with blindness of the left eye and temporal hemianopia with loss of central vision in the right eye. The left external rectus muscle was paralysed and there was right-sided hemiparesis affecting especially the face and tongue, the leg being practically unaffected. The pressure of the cerebrospinal fluid exceeded 300 mm., and its protein content was 60 mgm. per 100 c.c. An X-ray of the skull showed a faint shadow of irregular calcification in the left frontal region.

A left frontal craniotomy was performed by the late Sir Percy Sargent on December 4, 1931, but in spite of the relief of intracranial pressure vision became progressively worse. On February 5, 1932, a second operation was performed at which a mass of red tissue was seen emerging from the under surface of the left frontal lobe. In removing a nodule of this tumour for microscopy a large cystic cavity containing yellow fluid was opened. No further attempt at removal was made. The patient unfortunately died six days later from meningitis.

At the *post-mortem examination* made on the day after death it was found that practically all the tumour tissue had been removed at operation. The excised tissue had the typical histological characters of an oligodendroglioma. The nuclei were small, oval and of even size and most of them were surrounded by a narrow zone of unstained material. No mitoses were seen. These cells were separated from one another by a honeycomb of stroma which was seen under the oil immersion lens to be composed of knots and short strands of a material which stained terra cotta with van Gieson's counterstain and blue with Mallory's connective tissue stain. There was no collagen in the tumour except in the walls of the numerous small vessels which intersected it. Numerous calcified knots of irregularly spherical shape lay among the tumour cells; these had no relation either to vessels or to knots of collagen.

*Case* 2.—G. B., male, aged 44, was admitted to the National Hospital under the care of Dr. Grainger Stewart on January 6, 1932. He had suffered from depression for four months and later from mental apathy and confusion. Headaches had been present for about four weeks. On examination he was drowsy, inattentive, confused and disorientated. No papillœdema was present, the visual fields were full and the visual acuity excellent. The only physical signs found were slight left-sided lower facial weakness, and slight weakness and increase of tone in the flexor muscles of the left arm. The tendon reflexes in the left arm and leg were increased and the abdominal reflexes diminished on the left side, but both plantar responses were flexor in type. On January 12, the pressure of the cerebrospinal fluid was 115 mm.; the fluid was otherwise normal. An X-ray of the skull disclosed no abnormality. On January 17, he became progressively more drowsy and confused and rapidly sank into coma. The paresis of the left arm increased rapidly and there was an excess of extensor tone in both legs. Both plantar reflexes became extensor, and grasp reflexes, more pronounced on the right side, appeared. A lumbar puncture showed the pressure of cerebrospinal fluid to be now 300 mm. After magnesium sulphate enemata and two intravenous injections of 50 per cent. glucose consciousness returned.

On January 19, a right frontal craniotomy was performed by Mr. Donald Armour who opened a large cystic cavity under the second frontal convolution, midway between the frontal pole and the motor area. Some soft gelatinous tumour substance was found in the wall of the cavity and was removed. After the operation the patient improved and when discharged on February 24 he showed no abnormal physical signs but was still dull, apathetic and stupid.

On April 5 he had a generalized convulsion. On April 21 he became irrational, vomited blood, and was found to be paralysed down the left side. Thereafter he became more confused and disorientated, although the hemiplegia improved.

On readmission to hospital on May 2 there was still no papillœdema, and apart from a left-sided spastic hemiparesis the only added physical sign was horizontal nystagmus upon lateral deviation, slower upon looking to the left. On May 9 vomiting recommenced, he became more drowsy and more hemiplegic. Occasional jerking of the left arm was noticed. On May 21, Mr. Armour re-elevated the bone flap and revealed a large cystic tumour involving most of the white matter of the right frontal lobe. He removed a large mass of greyish gelatinous tumour and then closed the incision. The patient died twenty-four hours later without regaining consciousness.

*Histology of tissue removed at first operation.*—Several small pieces of tumour tissue, none larger than a pea, were sent to the laboratory for histological examination. In what appeared to be the more central parts of the tumour the tissue had a very cellular structure with an indefinite stroma in which oval vesicular nuclei lay apparently naked, no trace of a cell body being visible except round an occasional nucleus of rather different type. The majority of the nuclei were of uniform appearance, but in every field there were a few more darkly staining, irregularly shaped nuclei. Mitoses, chiefly of fairly regular type, were very numerous, two, three or more being present in every high-power field. In some parts of the tumour each nucleus was surrounded by a clear halo; in other parts most of the nuclei appear to lie on the fibres of the stroma, and only a few were in its meshes. These differences no doubt depended on the manner in which the individual small fragments had been handled and fixed. The stroma was composed of a lace-work of indefinite fibres which did not stain differentially by any special method. No astrocytes or neuroglia fibres could be seen in the central parts of the tumour, but at its margin they were fairly numerous. The numerous fine capillaries which ran straight or branched sharply were fed by vessels with fairly thick connective tissue walls. In some of these there was evidence of proliferation of the endothelium and a few thus became multicanalicular.

*Histology of tissue removed at second operation.*—A small flat piece of tissue was received for histological examination. In its histological appearance this bore a closer resemblance to a myxoma or a reticular astrocytoma of loose texture than to the tissue removed at the first operation. Many of the nuclei were now elongated, though most were oval or rounded. They were, however, more irregular in size, and small clumps of three, four or more nuclei were seen in many places. Most of the nuclei were still naked, but round many a small rim of cytoplasm could be seen which often streamed out into one or two long processes which merged with the reticulum. In places the meshes of this were wide and contained a structureless material which stained definitely with muci-carmine. In this were embedded a few rounded cells, many of which had fragmented nuclei. Where the network was more dense no such mucinoid material was present and there was more evidence of mitosis than of karyorrhexis.

Medium-sized vessels with fairly thick connective tissue walls were fairly abundant. In some places several small vessels of varying size were enclosed in a common sheath of thin connective tissue, and in such formations there was evidence of considerable endothelial overgrowth.

*Post-mortem examination.*—A post-mortem examination was performed three hours after death, the brain only being examined. The cavity from which the tumour had been removed contained a considerable quantity of blood-clot. Its walls were lined with a thin layer of tumour tissue which thickened up to about 1 cm. as it was traced mesially. Here the cavity communicated by a small opening with the lateral ventricle. A thin felt-like membrane, raised in some places into rather thicker cushions, lay on the inferior surface of the anterior horn of the ventricle. It passed down the foramen of Monro and was discernible as a slight opacity on the walls of the third ventricle. It was not visible in the iter of Sylvius, but there were traces of it in the fourth ventricle. The lower wall of the posterior horn of the right lateral ventricle was also covered by a fine membrane. The left cerebral hemisphere and the left lateral ventricle were free from any evidence of tumour.

Pieces of the tumour in the wall of the cyst were cut both in paraffin and celloidin. The membrane on the walls of the ventricles was studied in celloidin sections only. The appearance of the tumour as seen by the two methods of embedding presented considerable differences, and will therefore be described separately.

In *paraffin sections* the mural tumour differed from the pieces removed at operation. The majority of the nuclei were still naked, but less uniform in size and shape, and in addition to small oval nuclei larger, irregularly shaped or elongated forms and multiple nuclei were now abundant. A few astrocytes were seen with paler nuclei placed excentrically in a large cell body from which numerous fine processes were given off. The stroma was still reticular and for the most part stained undifferentially, but a few neuroglial fibres were also seen in most areas of the tumour. The distinction between the different elements in the stroma was well shown by Mallory's connective tissue stain which stained the cytoplasm of the astrocytes purple and their processes purplish red, whereas the reticulum as a whole was stained blue. That the latter was not of connective tissue origin was shown by its indifferent staining with van Gieson's and Perdrau's methods. The medium-sized vessels were chiefly of a glomerular or multicanalicular type. Mitoses were not quite so numerous as in the tissue removed at the first operation.

In *celloidin sections* of the mural tumour the matrix appeared granular rather than fibrous and neuroglial fibres could be seen only near its margin. Owing to the rather greater thickness of the celloidin sections (10 $\mu$), the nuclei seemed to be much more closely set, and in some places fairly solid bunches or elongated masses of nuclei were seen. Mitoses and karyorrhexis were abundant.

In the layer of tumour on the walls of the lateral ventricle the appearances were on the whole similar. Where the structure was more cellular the nuclei were uniformly rounded or oval with numerous mitotic figures, and neuroglial fibres were absent or very scanty. In other places, where the cells were more sparsely set, the nuclei were more elongated, and there was a fairly heavy feltwork of neuroglial fibres.

For the most part the tumour formed a zone of varying thickness under the ependymal layer, but in places it had burst through this, either as small granules or as wider cushions. The appearances of the smaller granules of growth bore a striking resemblance to those of syphilitic ependymitis, except that they contained no neuroglial fibres. In the wider cushions a few isolated neuroglial fibres had passed in from the subependymal layer of neuroglia.

In the fourth ventricle only small granules and a diffuse subependymal infiltration were seen. The condition here was very similar to the less involved areas in the lateral ventricles.

*Case* 3.—J. C., a boy aged 16, was admitted to the National Hospital under Dr. Grainger Stewart on February 14, 1932. He had suffered for eighteen months from attacks associated with jangling noises in the left ear, flashes of light to the left side and a sensation of trembling in the left arm. These were sometimes followed by unconsciousness or by a generalized convulsion. Headaches, vomiting and diplopia came on one month before admission. Slight aphasia had been present for five years, and this had recently become worse. On admission to hospital, there was definite left-sided "attention hemianopia," but the fields were normal to perimetry. Bilateral papillœdema and weakness of the right external rectus muscle were observed, although neither sign had been present on examination in the out-patient department three weeks earlier. There was slight left-sided lower facial paresis and a decrease in power in the left arm. The left abdominal reflexes fatigued more easily than the right, but the tendon reflexes and plantar responses showed no abnormality. There was slight loss of appreciation of position and passive movements, and some astereognosis in the left hand.

The cerebrospinal fluid was under a pressure of 320 mm.; it was otherwise normal. X-ray examination revealed a small faint shadow in the posterior part of the right temporal lobe.

In spite of enemata of concentrated magnesium sulphate solution, the patient became drowsier, the papillœdema increased and striate hæmorrhages appeared in the retina. Constriction of the left visual fields commenced, two-point discrimination on the left foot and the sense of position of the left great toe became faulty.

On February 22 following a generalized convulsion, there was left-sided spastic hemiparesis with hypæsthesia and hypo-algesia, and complete left homonymous hemianopia. He became progressively drowsier and daily intravenous injections of 100 c.c. of glucose were given.

On February 26 Sir Percy Sargent performed a craniotomy, exposing the cortex in the region of the right angular gyrus. The convolutions were swollen and fluctuated on palpation. A cyst containing 50 c.c. of yellow fluid which clotted on standing was opened in this region, and a cauliflower-like mural excrescence was removed from its anterior part.

The patient made an uninterrupted recovery. He returned to work but presented himself for examination in May, 1933, as he had recently had three fits. No abnormal physical signs could be found and there was no bulging at the site of operation.

*Histological report.*—The material removed at operation consisted of numerous small soft fragments of tumour, the histological appearance of which resembled somewhat that of a myxoma. The nuclei were small, oval or rounded and had an indefinite cytoplasmic body running out into processes which fused with one another to form a fairly loose network. These processes varied considerably in thickness and had very irregular and often ill-defined outlines, looking in fact much more like the result of coagulation of a viscid fluid than preformed fibres. They did not stain differentially by any method, remaining almost unstained with eosin, staining terra cotta with van Gieson's stain, blue with Mallory's connective tissue stain, and faintly pink with Mallory's phosphotungstic acid hæmatoxylin. They did not stain with Laidlaw's connective tissue stain. No mitoses were found in this tumour.

*Case* 4.—M. W., a girl aged 16, came under the care of Dr. Carmichael in the National Hospital on June 24, 1931. A year before admission she had been noticed to be walking unsteadily and five months later, when she complained that she saw "two of everything," her mother noticed that her right eye had turned inwards. After provision of glasses this symptom disappeared. Six months before admission she began to suffer from headaches which occurred at first monthly and later with greater frequency. They began upon waking in the morning, were compared to terrible pressure across the forehead and were associated during the one or two hours for which they lasted with distressing vomiting. During these attacks, in the later stages, she began to complain of momentary loss of vision in which everything went black. Her mother stated that the patient had always had a big head, that she had never menstruated and that, during the few months previous to admission, she had been listless and unable to concentrate.

The patient had a large head, characteristically hydrocephalic in shape and yielding a "cracked-pot" note upon percussion. She was of small stature and her secondary sexual characteristics were poorly developed. Her intelligence was slightly subnormal. Her visual acuity was $\frac{6}{6}$ on the right and $\frac{6}{24}$ on the left. The visual fields were full. There was bilateral papillœdema, the swelling measuring six diopters. A slight inequality of the pupils was the only ocular abnormality noted.

Examination of the limbs revealed a generalized hypotonia with signs of inco-ordination, slight upon the right, but definitely present on the left. The deep reflexes were equally active, the knee-jerks being increased and of pendular type. The superficial abdominal reflexes were absent, the plantars flexor. No sensory changes were detected. She walked upon a wide base in an ataxic manner.

After a ventriculography the patient developed severe headache and head retraction preceding unconsciousness, extreme collapse, and eventually death.

A *post-mortem examination* was performed less than twelve hours after death. Two flat plexiform neuromas were found, one on the inner side of the right thigh, and the other on the right occipital region of the scalp. The skull was large and very thin. On removing the brain the infundibular region of the third ventricle, which was distended and thin, tore across giving exit to a considerable amount of cerebrospinal fluid. There was considerable dilatation of the lateral ventricles.

Examination of the other organs of the body revealed little of note. The thymus was large, pinkish and firm, measuring 8 by 3 by 2·5 cm. and weighing 20 grm. The uterus was small. The ovaries however were full-sized and on section several ripening follicles were seen in them.

On section of the brain a greyish pink, rather gelatinous tumour was seen in the third ventricle filling the greater part of it, but leaving the anterior third free. It extended from the greatly dilated foramina of Monro backwards to the recessus pinealis, and downwards to the iter of Sylvius, into which a thin tongue of growth was protruded. It did not quite reach the recessus infundibuli, and it was covered on its anterior surface by a fine capsule. A narrow channel was thus left between the foramina of Monro and the distended recessus infundibuli. The supra-optic recesses were also distended. Some fine gritty particles were found in the anterior part of the tumour. The walls of the third ventricle were scarcely invaded by the growth, which was thus a small disc, only a few millimetres in thickness and scarcely more than 1 cm. in diameter.

*Histologically* it was composed of sparse rounded nuclei set in an indefinite matrix which, in paraffin sections, was separated from the nuclei, leaving a clear zone round each. Sometimes the clear zones round a group of several nuclei had fused together, so that the nuclei lay in an elongated space. Between these spaces the matrix consisted of an irregular and somewhat indefinite reticular tissue which stained a terra-cotta colour with van Gieson's counter-stain but blue with Mallory's connective-tissue stain. With muci-carmine and metanil yellow a great part of the reticulum stained bright red, especially near the nuclei, and many of the nuclei were ringed with a red halo. Where there was structureless exudate in the tissue spaces this also stained with muci-carmine. The walls of the vessels and the surrounding nervous tissue stained yellow and seemed to have no affinity for muci-carmine, nor was there any red staining in the immediate neighbourhood of the calcified granules. On the whole there was most mucinoid tissue in the central, looser parts of the tumour, but red staining of rings round the nuclei and of a fine meshwork between them could be seen in some places in the zone where the tumour was invading the walls of the ventricles. Numerous blood-vessels with thick walls which consisted of several endothelial layers and a thin connective tissue sheath, ran into the tumour from the periphery, being much more numerous near the edge of the tumour. A few small calcified knots lay in one part of the tumour, being set in the general matrix without any necessary relationship to the walls of the vessels or other collagenous structure.

The zone of demarcation between the tumour and the nervous tissue was everywhere fairly narrow, and in most places did not pass beyond the sub-ependymal layer of neuroglia. Where this zone was invaded there was always a considerable admixture of neuroglial astrocytes and their fibres, but apart from this zone no astrocytic nuclei and no neuroglial fibres could be seen in the tumour.

*Case* 5.—E. L., a woman, aged 50, was admitted to the National Hospital under the care of Dr. Gordon Holmes on May 30, 1932. She had suffered for seven years from headaches which were at first infrequent, and sometimes associated with vertically directed flashes of light in front of her eyes. Later the headaches became more frequent and were felt above the right eye and in the right temple. When they were severe she would feel nauseated and sometimes vomited. Three years before admission she complained of feeling unsteady on her feet when in the dark, and later this was also noticed in the daytime. She complained also of forgetfulness and of transient unpleasant smells, for which there was no apparent cause. One month before admission she was found under her bed unconscious and afterwards saw double for three weeks.

There was bilateral low-grade papillœdema, each eye having a visual acuity of $\frac{6}{12}$ and a normal field of vision. There was a variable left-sided lower facial paresis with protusion of the tongue to the left. The tendon reflexes of the left arm were slightly more active than those on the right and the left superficial abdominal reflexes were diminished. There was a slight but definite reduction in the appreciation of position and passive movement, in two-point discrimination and in stereognosis on the left side. She walked steadily but cautiously, and on first rising from bed she sometimes tended to fall backwards.

The cerebrospinal fluid was under an initial pressure of 270 mm. rising very slowly in the manometer. After removal of 4 c.c. of fluid the pressure rose very slowly to 70 mm. Bilateral jugular compression then caused a fairly rapid rise to 270 mm., the fall to 70 mm. consequent upon release of pressure being extremely slow. The fluid was yellow in colour and contained 0·40 per cent. of protein.

X-ray of the skull revealed an enlarged pituitary fossa with an erosion through its floor into the sphenoidal sinus. The sphenoidal ridge upon the right side was much thinned. Large vascular channels, in the position of the anterior branch of the middle meningeal vessels, marked the skull very deeply, particularly on the left side.

She died with symptoms of excessive intracranial pressure on August 9, 1932.

*Post-mortem examination.*—Twenty per cent. formalin was injected into the cisterna basalis through the orbit and into the cisterna magna within two hours of death. When the brain was removed next day a soft gelatinous mass of tumour was found in the supra-pituitary region. It had hollowed out the pituitary fossa, pushing the pituitary body down, but it had not destroyed the pituitary stalk. The posterior clinoid processes had been completely eroded and could not be seen. There was no capsule round the growth, and similar tumour substance was found on the ventral surface of the pons. Whether these growths were altogether subarachnoid could not be made out owing to the trauma occasioned by injection of formalin. There was considerable hydrocephalus with stretching and fenestration of the septum pellucidum.

On section of the brain in the median sagittal plane a soft gelatinous tumour, hæmorrhagic in its central parts, was found in the fourth ventricle, filling it and the iter of Sylvius and attached to the floor of the fourth ventricle which it appeared to penetrate for 1 or 2 mm. The third ventricle, like the lateral ventricles, was greatly dilated, and the infundibular region of its floor was ballooned out. There was no evidence of infiltration of the walls of the third or lateral ventricles by tumour.

*Histologically* the tumours in the ventricle and in the subarachnoid space were similar in character with minor differences. They consisted of an indefinitely fibrillar matrix, studded with small, round, darkly staining nuclei, around which no definite cell body could be seen. No mitoses could be seen. The matrix varied in appearance according to conditions of fixation and embedding. In the subarachnoid growth it consisted partly of a diffuse, rather granular substance, and partly, in paraffin sections, had shrunk into an indefinite reticulum enclosing clear spaces, some of which contained a structureless material which remained unstained with eosin, took a faint pink stain with van Gieson's counterstain, and stained fairly intensely with mucicarmine and with the aniline blue of Mallory's connective tissue stain. These staining reactions indicated its mucinoid character. The reticulum itself gave somewhat similar staining reactions, and its structure suggested that it was formed by shrinkage of a fluid mucinoid mass during the processes of fixation and embedding, rather than that it represented a pre-existing tissue. In the ventricular tumour the structure was similar in the parts furthest from the ventricular wall, and here also mucinoid exudate was present. But as one approached the wall there was an increasingly large admixture of fairly large astrocytes with long fibrous processes which passed for considerable distances in the matrix of the tumour. There was thus an intermediate zone where neuroglial fibres could be stained by differential stains (e.g., Mallory's connective tissue stain and phosphotungstic acid hæmatoxylin) in an indifferently stained matrix. This appearance was especially well seen in celloidin sections. There were numerous fairly thick walled vessels in the centre of the growth but in the more peripheral parts they were scanty and the walls of the smaller vessels consisted merely of endothelial cells. In the subarachnoid growths there were fairly numerous vessels with very thick walls of hyalinized collagen.

## DISCUSSION.

In his closely reasoned article Purdon Martin described two cases of oligodendroglioma and reviewed seventeen other cases which had appeared in the literature. He divided the cases into two groups, the first group of sixteen cases comprising those which lay laterally in the cerebral

PLATE VIII.

LIBRARY

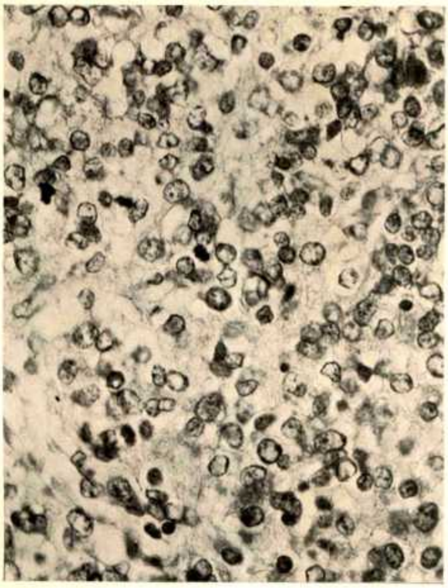

FIG. 1.

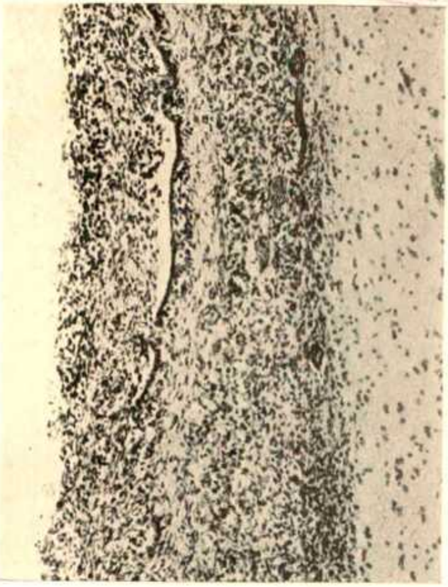

FIG. 2.

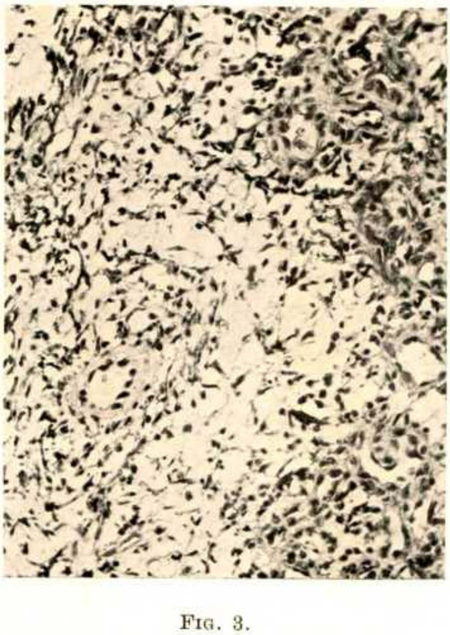

FIG. 3.

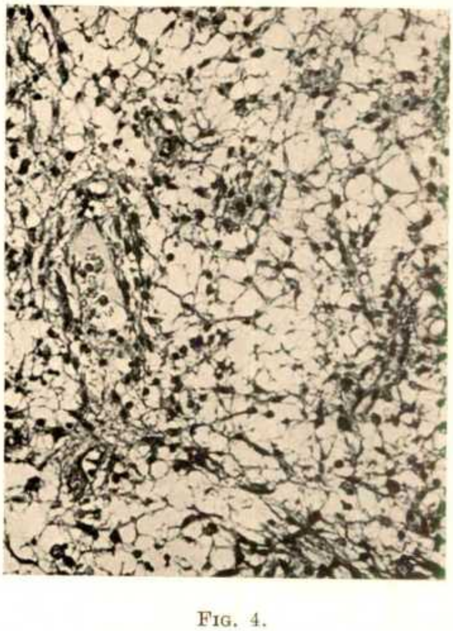

FIG. 4.

FIG. 1. *Case* 2.—High power view of tumour removed at first operation (paraffin section). The nuclei are rather less regularly arranged than in slower growing oligodendrogliomas. Two mitotic figures are seen.

FIG. 2. *Case* 2.—Low power view of growth on the wall of the lateral ventricle (celloidin section). The very cellular growth is seen both underlying and covering the ependyma. The junction of tumour with normal brain tissue forms an even line.

FIG. 3. *Case* 2.—Paraffin section of tumour removed at second operation which has a more myxomatous appearance than figs. 1 and 2. The greyish areas contain mucinoid exudate.

FIG. 4. *Case* 3.—Paraffin section of tumour removed at operation. Note the close resemblance to fig. 3.

*To illustrate Paper by Greenfield and Robertson.*

PLATE IX.

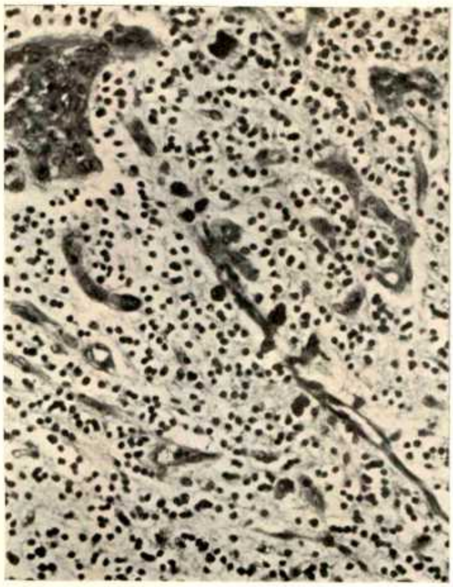

FIG. 5.

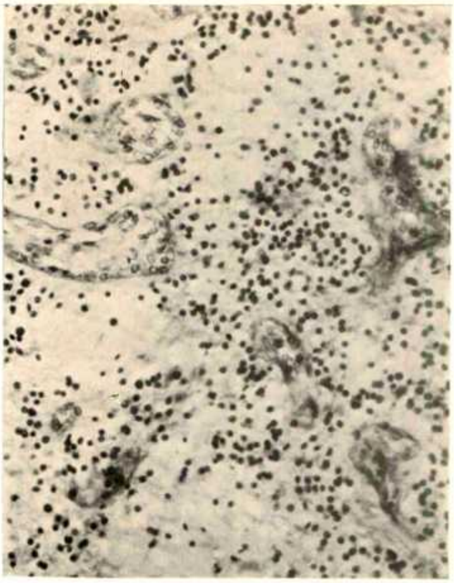

FIG. 6.

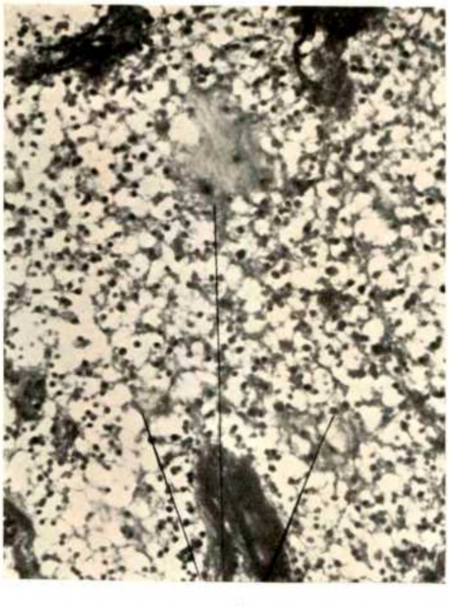

FIG. 7.

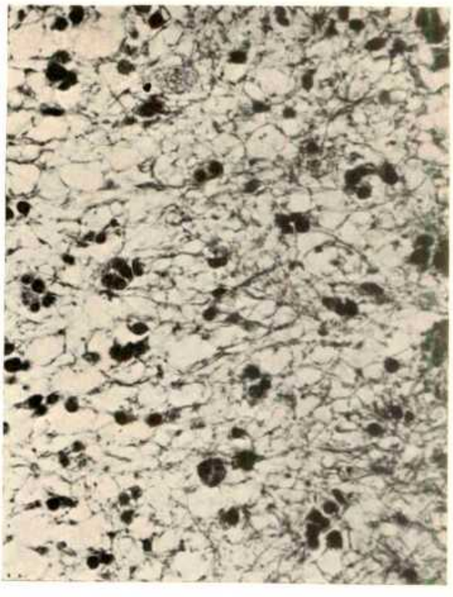

FIG. 8.

FIG. 5. *Case* 4.—Section of ventricular tumour showing regular small nuclei, most of which are surrounded by clear zones. Numerous calcified knots are seen grouped beside, and occasionally in, the walls of the blood-vessels. Hæmatoxylin van Gieson.

FIG. 6. *Case* 5.—Low power view of ventricular tumour (celloidin section), showing small nuclei of even size lying in a structureless stroma, with numerous vessels of fairly large calibre. Hæmatoxylin van Gieson.

FIG. 7. *Case* 5.—Ventricular tumour (celloidin section) stained with Heidenhain's Azan stain. In the original section the nuclei and some of the fibrillar stroma were stained red, the walls of the blood-vessels and the areas of mucinoid deposit (indicated by arrows *a*) stained blue.

FIG. 8. *Case* 5.—Tumour in cisterna basalis (paraffin section) stained with Mallory's phosphotungstic acid hæmatoxylin. Although a few dark purple staining (neuroglial) fibres are present in the section, the reticulum seen in the figure stains pink and contains no neuroglial fibres. The clumping of nuclei in small groups was only seen in this area of the section. Otherwise the section resembles figs. 3 and 4.

*To illustrate Paper by Greenfield and Robertson.*

hemispheres and th[illegible]econd smaller group those which lay in the mid-line of the brain. In the former group symptoms began late in life, on an average when the patient was 38 years of age, the extremes being 25 and 45. The tumours were invariably calcified, depending upon their much longer life history, and they produced symptoms, chiefly of an irritative nature, for a considerable period (on an average four years and eight months) before operation became necessary. Long periods of complete remission of symptoms were characteristic. "The primary operative results in nearly all cases were excellent." Cushing, however, remarks that the tumours often attain such a large size before operation becomes urgent that their complete removal is well-nigh impossible.

In Martin's second smaller group "The symptoms began at a much earlier age, the course was much shorter, there was no calcification in the tumours and the results of operation were unfavourable." He deduces from the difference in the age of onset of the symptoms in the two groups that the origin of the tumour is in most instances to be referred to the early adult life of the host, the mid-line group producing symptoms by obstructing the circulation of the cerebrospinal fluid, eighteen and a half years earlier than those placed laterally in the hemispheres. He concluded that the oligodendroglioma is a slow-growing tumour, liable to calcification and producing symptoms (unless mesially situated) only late in its life history when degeneration is occurring. Cushing's conclusions are similar, but in his last book he refers also to more rapidly growing tumours of this form.

The five cases here described fall readily, by virtue of their situation, into Martin's two groups. There was, however, considerable disparity of age in the two patients with mid-line tumours, one being 16 and the other 50. The three tumours located in the cerebral hemispheres all contained large cysts, and this cystic character may be correlated with the clinical history of the cases. The ages at which serious symptoms appeared in our cases were much more widely spaced than in the sixteen laterally placed tumours collected by Martin. In our youngest patient they appeared eleven years earlier than in his youngest, and in our oldest patient sixteen years later than in his oldest. In the cases of laterally placed tumours the total pre-operative course is much shorter than the average (four and three-quarter years) of the collected series. The youngest patient had the longest clinical history of seventeen months, the next oldest had been ill for four months, and the oldest for eight months; had the last patient not refused operation this period would have been much shorter. (In this case the rapid failure of vision, due to direct pressure of the cystic tumour on the left optic nerve and tract, was an additional cause for operative interference.) This short preoperative course and rapid onset of symptoms of increased intracranial pressure must be due to increased rate of expansion of the tumour or of a cyst associated with it.

The second case affords the most striking example of the rapidity of onset of symptoms of intracranial pressure. The pressure of the cerebrospinal fluid was 115 mm. four days before the onset of confusion, coma and bradycardia; these physical signs were associated with a rise of intracranial pressure to over 300 mm. In the third and youngest patient symptoms of increased intracranial pressure were present for only five weeks, and papillœdema for only four weeks, before the onset of serious symptoms necessitating treatment by dehydration. In each of these two cases the administration of intravenous glucose solution was a valuable pre-operative measure.

Only one of these three cases showed irritative symptoms, and these accurately localized the tumour, which apparently arose in the region of the right angular gyrus. The other two tumours were situated in the frontal lobes, and their symptomatology was dependent on destruction of cerebral tissue and local and general pressure. Martin, reasoning from the evidence before him, suggested that calcification occurs during the later years of the life history of the tumour when it is undergoing degeneration. Yet in the cases here described the X-ray in the patient of 16 years showed a localized area of calcification, and calcareous deposits were found histologically in the intramural nodule. The frontal tumour of the patient aged 44 showed no calcification.

On the other hand our two cases of mid-line tumour had long preoperative histories. The hydrocephalus in Case 4 had been present since infancy and at the time of examination it was of considerable degree with the typical cracked-pot note on percussion of the skull and a beaten silver appearance and separation of sutures on X-ray examination. At the post-mortem examination the only obvious cause for the hydrocephalus was the tumour, which therefore had probably been present since infancy. In Case 5 a definite history of symptoms for seven years was given. If we allow for the relief of pressure which would be provided for by the expansion of a child's skull, this period becomes comparable to the duration of the hydrocephalus in Case 4. These two small ventricular tumours are thus remarkable instances of the slow rate of growth of some oligodendrogliomas.

The operative results in these cases were almost uniformly bad.

The first case died of septic meningitis after a two-stage attempt at removal. This was the more unfortunate as the post-mortem examination showed that the removal was almost complete. The rapid recurrence of symptoms in Case 2 necessitated a second operation four months after the first. Had he survived this operation death could not have been long delayed by reason of the extensive ventricular spread. Our third patient has remained well until the time of writing, fifteen months after his operation. Surgical removal of the two ventricular tumours was not attempted.

An interesting point may here be raised in connection with the cerebrospinal fluid findings in Case 5 which may be interpreted as the result of increased intracranial pressure, combined with a block in the communication between the fluid in the ventricles and that in the subarachnoid space. The very slow rise of fluid in the manometer to a high initial pressure, the slow pressure changes (especially marked being the very slow fall after release of jugular compression), and the yellow fluid with high protein content, may be of considerable importance in the diagnosis of a tumour of the fourth ventricle.

On the *pathological side* these cases present certain features which, although not new, merit more attention than has been paid to them in the past. The first to which we wish to draw attention is the alteration of tumour type from that of a typical and easily recognizable oligodendroglioma, to that of a reticular tumour containing mucinoid substance in its meshes. Martin described and figured the appearances of the ventricular metastases in one of his cases in which a similar reticular structure was seen. He did not, however, find evidence of mucinoid substance in the meshwork of the tumour. To this latter point Roussy and Oberling have drawn attention in their atlas, and their illustration shows cells of elongated form resembling Penfield's piloid astrocytes, embedded in a solid matrix which stains pink with mucicarmine. But there is here very little suggestion of a network of processes such as we found in Cases 2 and 3. Although they do not adduce such direct evidence of relationship as Martin and ourselves have done, it is probable that Roussy and Oberling are justified in linking their "mucous glioma" to the oligodendrogliomas. The network is probably, as Martin suggested, partially artefact (i.e., the precipitation and shrinkage of a colloidal matrix and for this reason most evident in paraffin sections), and partly the result of the growth of the tumour in a cavity where there is nothing to prevent the separation of the cell bodies from one another. The latter supposition would explain the different appearance of the mural nodule removed at the second operation in Case 2 from that found at the first operation, for this nodule must have grown into a pre-existing cyst. At the same time the histology of this nodule seemed to explain the formation of mucinoid material as a degeneration product of the tumour cells, since it was most abundant in areas where degenerative changes in the nuclei were most in evidence. Bailey and Bucy have drawn attention to this point, and, following Grynfeltt, Pelisser, and Bailey and Schaltenbrand, consider that mucinoid substance is produced by degeneration of oligodendroglia.

The second point is the character of the stroma or reticulum in oligodendrogliomas. This appears with low magnifications, in paraffin sections at least, to consist of fine fibres which form a honeycomb or network in which the cells lie. But with higher magnification and suitable staining it is possible to see that this apparent network is not formed of continuous fibres but of interrupted rods and granules. When the tumour grows into the cavity of a cyst or free on the walls of the ventricles, fairly definite fibres appear even in celloidin sections, although, as has been noted, these may be to some extent artefact. The staining reactions of this material also are of interest, in that it always takes the indifferent stain with mixtures of anilin dyes, orange with van Gieson's counterstain, and blue with Mallory's "connective tissue" stain. The latter is a valuable differential stain for neuroglia fibres which it stains purple, and in most gliomas it stains nothing blue except the connective tissue of the vessel walls. In oligodendrogliomas, on the other hand, much of the reticulum stains blue, although one can see a few neuroglial fibres in some parts of the growth, especially where it is invading the brain.

Roussy and Oberling seem to have missed this point in their atlas in which they describe the fibres which stain with anilin blue as collagen. That the reticulum is not of connective tissue origin is shown by its failure to stain by Perdrau's method. We therefore lay some stress on the use of Mallory's "connective tissue" stain and its derivatives such as Masson's trichromic method or Heidenhain's "azan," in distinguishing oligodendrogliomas from other forms of glioma.

It seems probable that this characteristic stroma in oligodendrogliomas is closely related to the mucinoid material which results from the degeneration of oligodendroglia cells. It is stained faintly with mucicarmine, and its reactions with Mallory's connective tissue stain and with Heidenhain's azan are similar to those of mucin. Further, its appearance as granules or short irregular strands suggests precipitation during fixation from a substance in a fluid state.

Unfortunately, we were unable in this series of cases to stain oligodendroglia selectively by silver carbonate. The fragments removed at operation were very small and soft and did not allow of frozen sections. And in the post-mortem material the method gave uncertain or negative results, as is usually the case. We had therefore to rely for our diagnosis on the general histological picture of the tumours and on the reactions of their stroma to anilin dyes. In Case 2 our failure to demonstrate oligodendroglia fibres by silver staining may lay this diagnosis open to doubt, and as the diagnosis in Case 3 to some extent hinges on that of Case 2, our reasons for the latter diagnosis may be recapitulated. First, the original operation material was diagnosed from its general histological appearance and staining reactions as coming from a rapidly growing oligodendroglioma. The structure of the material from the second operation, although reticular, was very different from that of any astrocytoma, and was in fact not unlike that of a myxoma. But a comparison with the material from the first operation showed more similarities than were apparent at first sight. The differences were indeed easily attributable to conditions of growth in a cystic cavity.

The post-mortem material resembled the tissue removed at the first operation rather than that taken at the second, although the interval between the latter operation and death was only a few hours. But almost all the tumour on the walls of the cavity represented the growing edge, where tumour was invading normal brain tissue, and therefore contained a large admixture of neuroglial fibres. Only in one or two places could the tissue be considered to consist solely of tumour cells, but in these the resemblance to the tumour removed at the first operation was very close. To the naked eye also the post-mortem tumour resembled an oligodendroglioma much more closely than any other form or glioma. Although it was invading the normal brain round the walls of the cavity, its margin was well defined and was more or less concentric with the cyst wall, although the thickness of the layer of tumour varied in different parts. Another point of resemblance to oligodendrogliomas was that, in spite of the malignant appearance of the tumour at the time of the first histological examination, it had not attained any great size when the patient died four months later. It was nowhere as much as 2 cm., and in most places only a few millimetres, in thickness.

The growth on the ventricular walls resembled very closely that seen in Martin's Case 2, and was to us another point in favour of the diagnosis of oligodendroglioma. In our case, however, we appeared to have an earlier stage in ventricular metastasis, and no such large masses were found as were seen in Martin's case. Particularly similar was the diffuse infiltration which covered the lower parts of the ventricular walls and which appeared to spread centrifugally from the main tumour mass. This resemblance was perhaps greater to the naked eye than on microscopic examination, as in our case the growths were more subependymal than free on the surface, but where the tumour had penetrated the ependyma the similarity was fairly close.

The occurrence of oligodendrogliomas as primarily ventricular growths was indicated by Carnegie Dickson in 1926. Cases 4 and 5 are very characteristic examples of this. In both the history was a long one. If we are to attribute the hydrocephalus in Case 4 solely to the tumour, the latter must have been present for about fourteen years, but it was still little more than the size of a broad bean at death. There can be little doubt as to the diagnosis in this case, as the appearance of the tumour, including the knots of calcification in the matrix, was typical enough. As in Case 1 these had no relation to any collagen. Case 5 is of special interest owing to the presence of a subarachnoid metastasis in the basilar cistern. The growth here had a reticular appearance very similar to that removed at the second operation in Case 2, and to the intracystic tumour in Case 3. Mucinoid degeneration had taken place in both these ventricular tumours probably owing to the scanty blood supply, but in neither were there mitoses or evidence of rapid growth. In fact both the history and the appearance of the tumour in Case 5 indicated a slow rate of growth, in spite of the absence of calcification. We appear therefore to have in this case an instance of metastatic spread along the cerebrospinal fluid pathways in an oligodendroglioma of slowly growing type. This is probably of very rare occurrence. Both in Martin's Case 2 and in our Case 2, ventricular spread occurred from a tumour which showed many mitotic figures and gave other evidence of rapid growth. The spread from the fourth ventricle to the basilar cistern probably took place through the foramina of Luschka, as there was no evidence of tumour in the region of the cisterna magna. The distance to which the tumour had spread would thus be only one or two centimetres. Spread to the subarachnoid space from a spinal tumour is described by Kernohan, but he does not make it clear whether this was of slow or of more rapidly growing type.

## SUMMARY.

Five cases of oligodendroglioma of the brain are described. Three were cystic tumours of the cerebral hemispheres, and two were mid-line ventricular tumours.

No age distinction can be made between laterally and medially placed tumours of this type. The former occurred in patients of 16 to 61, and the latter in patients of 16 and 50 years of age.

While a small medially placed tumour, by blocking the exit of cerebrospinal fluid from the ventricles, may produce as severe symptoms as a larger laterally placed tumour, the great variation in the ages of our patients is evidence that the tumours may begin to grow at any age-period.

The tendency to calcification in oligodendrogliomas bears little relationship to the age of the host. Calcified knots were found in the tumours in our two patients of 16. In this series of cases they occurred in the stroma of the tumour and were not related to the walls of blood-vessels or other connective tissue.

The short pre-operative histories and the rapid onset of urgent symptoms in our cases of laterally placed tumours were related to the expansion of cysts associated with slowly growing tumours.

The rate of growth and malignancy of these tumours vary from case to case. Cases with ventricular and subarachoid metastases have been reported, and we have described further instances of both methods of spread.

An oligodendroglioma growing in the wall of a cyst or in a cavity may alter its histological appearances, assuming a more myxomatous type. Under these conditions of growth it is particularly liable to give rise to a mucinoid exudate which may form large accumulations. The reticular appearance seen, especially in paraffin sections, appears to arise largely from shrinkage of this mucinoid material.

We desire to express our thanks to the honorary medical staff of the National Hospital for permission to use the records of these cases.

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# THE PRESENCE OF EFFERENT FIBRES IN POSTERIOR SPINAL ROOTS.

BY SIDNEY KAHR, B.S., M.D.,
*New York City,*
AND
DONAL SHEEHAN, M.D., M.Sc.,[1]
*Manchester.*

(*From the Neurological Institute, University of Vienna: Director-Professor O. Marburg.*)

## INTRODUCTION.

THE question of the existence of efferent fibres in posterior spinal roots has engaged the attention of many investigators since the enunciation of the Bell-Majendie law. The presence of such efferent fibres in several of the lower vertebrates has been well established, but it is still a controversial point whether they exist in the higher mammals. The possibility of the existence of this disputed system of fibres is of great anatomical interest and provokes far-reaching physiological implications. The belief that such fibres did not exist in the posterior root in part led Bayliss to formulate the law of antidromic action in explanation of the vasodilatation which occurs on stimulation of the cut peripheral stump of the posterior spinal root. Later Kuré attributed trophic functions to these fibres, and he believes that the ætiology of progressive muscular dystrophy is to be sought in lesions of this efferent system. Pathological changes in his so-called "spinal parasympathetic" nervous system are mentioned by Kuré and his co-workers in cases of tabes, syringomyelia, leprosy and sclerodermia. Kuré believes that the trophic changes are only in part dependent on the circulatory disturbances resulting from involvement of these efferent fibres.

If the presence of efferent fibres in posterior spinal roots can be firmly established, the questions of a trophic centre, of its central and spinal connections, and of a possible relay station in the spinal ganglia will naturally arise. In the present study we have confined our attention to a purely anatomical consideration of the problem.

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[1] Research Student on the Dickinson Travelling Scholarship in Medicine.

## LITERATURE.

That vasodilatation occurs on mechanical and electrical stimulation of the peripheral stumps of cut posterior spinal roots was first shown in dogs by Stricker (1877), and this has been since confirmed by many investigators, including Gärtner (1889), Hasterlik and Biedl (1893), Bayliss (1900) and Langley (1923). More recently Foerster (1929) has demonstrated vasodilatation in man on stimulation of all the posterior roots, from the high cervical to the lower sacral, and he has shown that the area of vasodilatation has a strictly dermatomal distribution.

As far back as 1887 Bornezzi, from physiological experiments, came to the conclusion that vasodilator fibres run centrifugally in all the posterior roots, but histological evidence in support of this physiological deduction did not appear until some time later. Previously Kutschin (1863) had shown from his study of Petromyzon that posterior root fibres arise from posterior horn cells and from small cells which lie between the anterior and posterior horn. This observation was confirmed by Freud (1879), who demonstrated in this animal that two-thirds to three-fifths of the fibres in the spinal ganglion are not in communication with the spinal ganglion cells. It must be remembered, however, that the posterior horn cells in Petromyzon are bipolar and resemble those of the spinal ganglion, a vestigial condition where some of the cells properly belonging to the posterior root ganglion are situated in the spinal cord.

Ramon y Cajal (1890) and Lenhossék (1890) were able to demonstrate in the chick embryo efferent fibres in the posterior roots, fibres which spring from the posterior part of the anterior horn and pass through the posterior root and spinal ganglion without connection with bipolar cells of the latter. Lenhossék also observed the presence of these efferent fibres in a vertebrate, but he does not state the species, nor does he offer histological evidence of these findings. Van Gehuchten (1893) confirmed Cajal's and Lenhossék's observations, and agreed with the latter workers as to the "motor" nature of these fibres. Working on mammalia, Vejas (1883), after tearing out anterior and posterior roots, observed that the central stumps disappeared. The operative procedure permits possible extensive damage to the cord and makes the drawing of definite conclusions unwarranted. Joseph (1887), using cats, cut the second cervical nerve between the ganglion and the cord, and six to eight weeks later examined the stumps after staining with Marchi and osmic acid. He observed a few degenerated fibres in the ganglion and in the peripheral nerve, and from his experiments concluded that from the spinal cord a number of fibres arise and traverse the posterior root ganglion without entering into any relationship with the bipolar cells. The possibility of retrograde Wallerian degeneration and the failure to report the condition of the central stump open his work to criticism. Singer and Münzer (1890), and Kölliker (1893), and others, were unable to confirm the findings of Vejas and Joseph.

Sherrington (1894-95), operating on cats and monkeys, examined the distal and proximal ends of the cut posterior roots after section between the cord and the ganglion. He used osmic acid as the stain. In some of his experiments the anterior roots were also cut, and in others the spinal ganglion was excised. The time allowed for degeneration varied from nine to forty-two days. Sherrington concluded that his observations confirmed the original observations of Waller, that in the posterior roots no fibres pass from the spinal cord outwards to or through the spinal ganglion; all pass towards the spinal cord. These conclusions are, however, rather ambiguous, for in two of his experiments on cats, where the spinal ganglia had been also excised, the spinal ends of the cut posterior roots showed a number of small intact fibres. He states, "further examination revealed great numbers of extremely delicate myelinated fibres varying from 1 μ to 3·5 μ in diameter. These possessed perfect continuity and were clearly not degenerating. They were scattered throughout the whole thickness of each root. They much resembled young regenerating fibres. . . . Inasmuch as the spinal ganglia had in this experiment been in each case actually excised it is difficult to understand how regeneration of any root fibres could have occurred." In discussing the nature of these intact fibres, Sherrington writes, "I cannot explain the presence of the minute myelinated fibres in the spinal portion of the dorsal (posterior) root five weeks after excision of the ganglion. In the course of the second and third weeks I have not found them. Their existence is beyond question, as also the completeness of excision of the ganglia, which were preserved at the time of operation. I reserve discussion of their origin until a subsequent paper." This work was performed on the lumbosacral nerves. In a later work on thoracic roots, in a cat and two monkeys, Sherrington (1897) examined the proximal stumps (on an average fourteen days later), and found "every fibre was in a state of advanced degeneration." He concludes, "In these animals, therefore, eleven dorsal (afferent) spinal roots, taken from the region of the cord whence arise the efferent fibres of the sympathetic system, do not contain any nerve-fibre possessing an intraspinal origin."

On the basis of the assumption that there is no definite histological evidence of the presence of efferent fibres in the posterior roots in mammals and on the results of physiological experiments, Bayliss (1900-01) postulated his theory of "antidromic" action. He accepts Sherrington's conclusions, and mentions also the fact that he has been able to confirm them with respect to the lower lumbar roots of dogs. He also regards as conclusive the work of Singer and Münzer (1890), Münzer and Wiener (1895), and Kohnstamm (1899), who were unable to confirm Joseph's findings in the mammal. In his physiological experiments Bayliss divided the lower lumbar and first sacral posterior roots in seven dogs close to the spinal cord. Eight to fourteen days later he stimulated the peripheral cut ends of these roots and still obtained vasodilatation. In another series of experiments he removed the complete lumbar cord, and eight days later stimulated a mixed nerve and obtained no muscular twitchings (proof of the degeneration of the anterior component), but vasodilatation ensued. He concluded "that the vasodilator fibres of the posterior roots, whatever be their nature, do not degenerate on section between the posterior root ganglion and cord, so that they are not spinal efferent fibres." Later he demonstrated that they do degenerate when the posterior root ganglia are extirpated and that hence their trophic centres are in these ganglia. These conclusions are only valid on the acceptance of the fact that the fibres described by Cajal and Lenhossék, and by Joseph in mammals, traversing the spinal ganglia without entering into any relationship with the bipolar cells, are the efferent vasodilator fibres in question. Kuré (1931), however, as will be seen later, believes that these efferent vasodilator fibres, arising from cells in the spinal cord and traversing the posterior roots, possess a relay station in the spinal ganglion. If this is true, the results of Bayliss' physiological experiments are compatible with the presence of these fibres, without the necessity of hypothecating antidromic impulses.

Lugaro (1906), sixty days after removal of spinal ganglia in dogs, found in the posterior root fine "regenerated" fibres and rarely normal fibres. He mentions the possibility of regeneration occurring by invasion of fibres from the anterior root. However, he presents no histological evidence for this, and is more inclined to the view of autoregeneration.

Ranson (1914), in a series of ten cats, ligated or cut the anterior and posterior lumbo-sacral roots proximal to the ganglion. The period allowed for degeneration was fourteen to seventy-four days. He studied the proximal stumps after staining with Marchi, Pal-Weigert, and pyridine silver. Almost all the fibres in the posterior root as it enters the cord were degenerated. However, in five cats, the sections of which were stained by pyridine silver, a small number of fine axons of normal appearance were found entering the cord. In two other cats a few fine medullated fibres of normal appearance were seen entering the cord from the degenerated roots. In two of the cats of the first series, twenty-four days after the roots had been tied, some of the fine axons in the dorsal roots were branched, but the end bulbs typical of regenerating fibres were not seen. He emphasizes the fact that these fibres were much more abundant near the cut end of the root but some could be clearly traced in the root as it entered the cord. Ranson concludes "there can be no question but that the presence of great numbers of these fine axons in the degenerated roots can only be explained on the basis of their being regenerated. But it is not easy to decide how to regard those few axons that end beyond the transition point into the cord. It is possible that they are efferent fibres and it is equally possible that they are regenerated fibres." Ranson regrets that the spinal ganglia were not removed in this series of experiments so as to exclude the possibility of regeneration. " Only by excluding this possibility can the question of efferent dorsal root-fibres be settled" (1929). In this later paper, Ranson, discussing the same experiments, remarks that the time which had elapsed before study was sufficient for the appearance of regenerating fibres.

Kuré (1931) and his pupils approached the problem from the aspect of the tonic autonomic innervation of striated muscle; Frank (1921) had previously supposed a parasympathetic tonic innervation of striated muscle and concluded that it reached the muscles by way of the posterior roots. As the nature of our problem is purely histological we only propose to discuss the evidence brought forward by Kuré and his co-workers for the existence of efferent fibres in the posterior roots. In a large series of dogs he sectioned cervical, thoracic, lumbar and sacral posterior roots between the spinal ganglion and the cord, and then studied the proximal and distal stumps after staining with the Weigert-hæmatoxylin method. Varying periods of time, extending to several months, were allowed for complete degeneration. Kuré found in the proximal stumps a great number of intact finely myelinated fibres, 75 per cent. of which were 1 to 3 $\mu$ in diameter. The numbers in the different roots were variable; and always there was a disparity, often a striking one, between the greater number in the central stump and the corresponding fibres in the distal stump. Upon the persistence of finely myelinated fibres in the proximal stump, and the appreciably smaller number in the distal stump, Kuré in part bases his evidence for efferent fibres in the posterior root.

As Kuré did not apparently remove the spinal ganglia, it is evident that regeneration in the distal stump may have occurred from an intact ganglion. Ranson demonstrated that this happens (1914). Since regeneration of myelinated fibres occurs (Ranson) after fifty-four days and Kuré's studies were usually made after longer periods, extreme variability in the number of fine medullated fibres in the distal stump would be expected. This fact casts doubt upon the uniformity of the figures given by Kuré.

His co-workers, in particular Kawaguzi (1931), studied the cord with Nissl stain following section of the posterior roots. They claim to find constant changes (retrograde) in the small cells lying between the anterior horn and substantia gelatinosa. They state that these cells are similar to the autonomic cells in size and shape, but show no changes after extirpation of the sympathetic cord, and further that their number corresponds closely with that of the finely myelinated fibres in the posterior root. The retrograde changes in these cells following section of the posterior root are given as presumptive evidence that the efferent fibres in the posterior roots (called by Kuré the "spinal parasympathetic system") arise from these cells. Unfortunately Kuré's photomicrographs are unsatisfactory and unconvincing. On the basis of the fact that the cranial parasympathetic fibres have a relay station in a distally situated ganglion (pre- and post-ganglionic neurones), Kuré assumes that his "spinal parasympathetic fibres" relay in the spinal ganglion without offering any histological evidence for such an assumption. That multipolar cells do exist in the spinal ganglia has been shown by Dogiel (1896) and many others, but that these cells are in direct relationship with efferent fibres in the posterior roots is as yet unproven.

Previous work on cellular changes following posterior root section had been done by Warrington (1898), Spiller (1900), Lapinsky (1907), and Timasheff (1911). Warrington cut several posterior roots from the fifth to the ninth thoracic, using the intradural approach, and noticed a marked alteration in the cells of the postero-external group of the anterior horn, but these were also observed to a lesser degree on the opposite side. Warrington considered that the changes were the result of the "withdrawal of the afferent impulses which normally impinge upon the anterior cornual cells." Spiller found no distinct alteration of the cells of the anterior horn following posterior root section in three cats. Lapinsky experimented on dogs and used the extradural route. Usually only one, occasionally two, posterior roots were cut. Two to four weeks later he was able to see pathological changes of several of the cells in Clarke's column, and to a lesser extent in the anterior horn. Unfortunately the anterior root also showed a considerable degree of Marchi degeneration, so that the results cannot be finally accepted as entirely due to the posterior root lesion. Nor is his evidence that the proximal stump of the posterior root appears completely degenerated sufficient to exclude the possibility of intact fibres remaining, since such fibres would be with great difficulty recognizable in Marchi preparations. Timasheff cut lumbar posterior roots in dogs, and after a period of three to fifteen days studied the distal stumps in preparations stained by Marchi. He found that about 5 per cent. of the fibres underwent degeneration. Nissl preparations of the cord showed chromatolysis in some of the cells of the corresponding segments, chiefly in the anterolateral parts of the anterior horn. Such changes were to be observed mainly in the grey matter of the same side, but also to some extent in that of the opposite side. Timasheff concluded from his results that centrifugal fibres exist in posterior roots.

Gagel (1930A) has examined the central stumps of severed posterior roots in man in eight cases, on which posterior rhizotomy had been performed by Foerster. In one of these, five years had elapsed since the time of the operation. In all cases the central stump was cut serially and stained for myelin sheaths. In every case Gagel found many finely myelinated fibres, and in the zone of the cord where the root enters these could be clearly seen, though it was not possible to trace them far. It is interesting that these fibres were more numerous in those patients who had survived the operation for longer periods. Gagel considers this may be due to radiculitis, or that individual variations might explain it. He concludes that there is no question of the existence of these finely myelinated fibres in the proximal stump in man, that they are clearly anatomically efferent, but that there is still no clear proof of their physiological function.

Gagel (1930B) also examined the spinal cord with the Nissl method in human material and from two monkeys in which posterior roots had been divided by Foerster. He observed changes in the cells of the intermedio-mesial group of the anterior horn and in the large cells of the posterior horn, at the level of the divided root. Similar changes were to be seen in the cells of Clarke's column on both sides of the cord, but at a level one or two segments above the site of operation. He concluded that the retrograde cell changes observed were in part "trans-neuronal."

Selle (1930), working at Müller's clinic, gives a clear résumé of Kuré's work and is entirely in agreement with his findings.

Tower (1931), in a search for trophic influence of posterior spinal roots on skeletal muscle, operated on four cats, sectioning the posterior root in one segment (lower cervical and upper dorsal) proximal to the ganglion, and combining the operation with a complete excision of the corresponding spinal ganglion. The animals were left four, six and twelve months respectively. The central stumps of the posterior roots in these experiments were stained by Marchi, Weigert-Pal and Bielschowsky. Her study of the central stumps showed numbers of fine nerve-fibres, 2-3 μ in diameter, the majority unmyelinated after four months, but after one year many, if not most, were thinly myelinated. They were most numerous in the cat, which was allowed to survive twelve months after the operation. Some of these fibres penetrated the spinal cord along the blood-vessels, but none probably through the root zone proper. In the latter area the entering fibres were surrounded by neuroglia, and some fibres were seen to terminate in a small growing knob. Since the posterior root ganglia (and the sympathetic also in one case) were completely excised, Tower concludes that the ventral root must be the major source of the fibres invading the vacated posterior root stumps. Many of the fibres could be actually directly traced from the ventral roots. The ventral root-fibres involved in this regeneration were chiefly the superficial layer adjacent to the cicatrix, i.e., those probably damaged at the time of operation. "The nerve-fibres found in the proximal stumps of severed posterior roots, and described by Kuré as spinal parasympathetic, are regenerating fibres from the ventral root. They neither enter nor emerge from the cord, except a small fraction which utilize the perivascular connective tissues as a route of entry."

The most recent criticism of Kuré's work has been advanced by Kiss (1932). By a prolonged osmic acid stain, he has examined the cranial spinal and sympathetic ganglia in various vertebrates, and has confirmed the presence of multipolar "sympathetic" cells in the spinal ganglia. He concludes that the effective (centrifugal) fibres of the posterior spinal roots are preganglionic fibres of these sympathetic cells. Kuré considers them the parasympathetic preganglionic fibres of cells situated in the same spinal ganglion, from which the postganglionic fibres pass to their peripheral destination sometimes through the

# PLATE X.

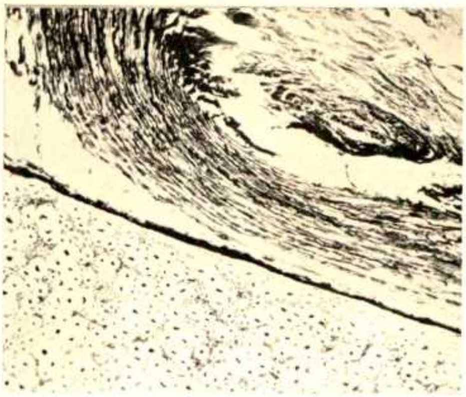

FIG. 1A.

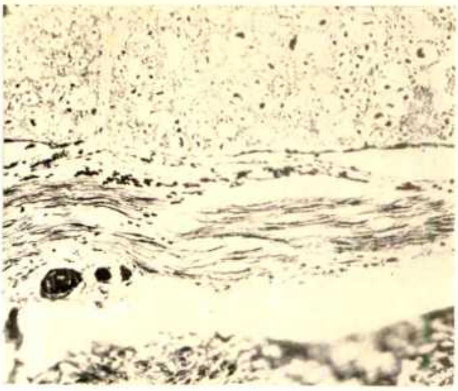

FIG. 1B.

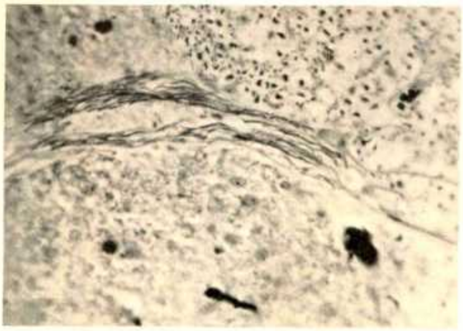

FIG. 2.

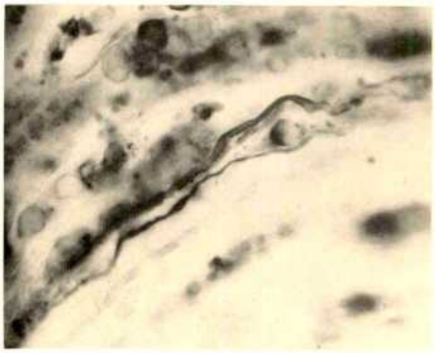

FIG. 3.

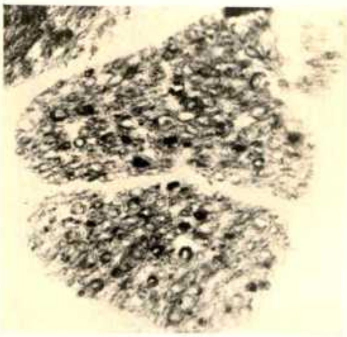

FIG. 4.

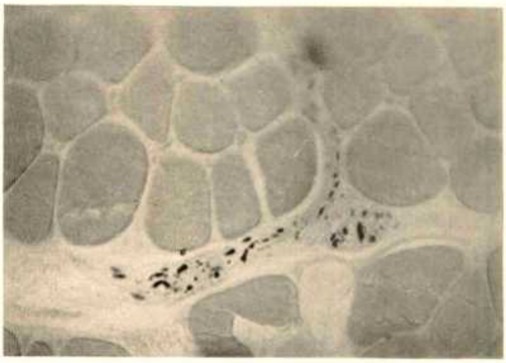

FIG. 5.

FIG. 1.—Longitudinal sections of posterior root (Bielschowsky), showing contrast between (*a*) normal side and (*b*) operated side. (*b*) shows intact axis cylinders with occasional degenerated fibres still to be seen. Sixty-nine days after posterior and anterior root section and excision of spinal ganglion. × 120.

FIG. 2.—Intact axis cylinders arching into the base of the posterior horn (Bielschowsky). Forty-five days after posterior and anterior root section and excision of spinal ganglion. × 225.

FIG. 3.—Normal myelin sheaths in posterior root (Weigert). Thirty-six days after posterior and anterior root section and excision of spinal ganglion. × 300.

FIG. 4.—Transverse section of distal end of cut posterior root (Marchi), showing degenerating myelin sheaths. Fourteen days after intradural posterior root section. × 120.

FIG. 5.—Myelin sheath degeneration in small nerve bundle in muscle (Marchi). Fourteen days after intradural posterior root section. × 135.

*To illustrate Paper by Kahr and Sheehan.*

### PLATE XI.

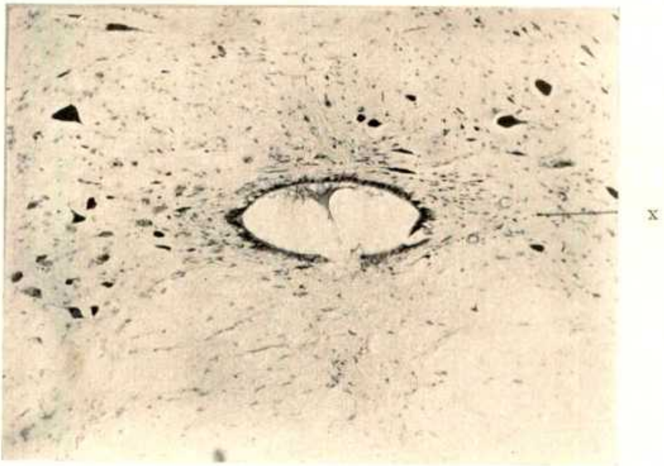

FIG. 6.

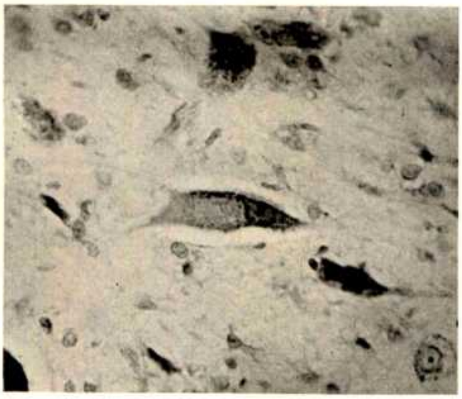

FIG. 7.

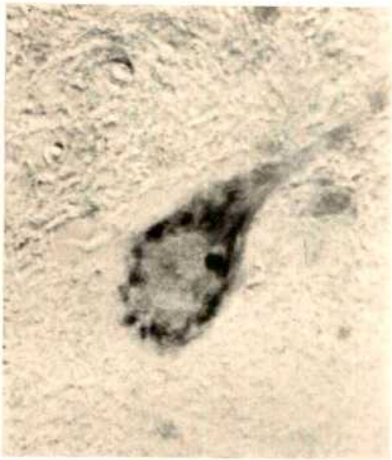

FIG. 8.

FIG. 6.—Intermediate zone of spinal cord (Nissl). **x**, operated side, and shows diminution in number of these cells. × 66.

FIG. 7.—Typical large cell from the intermediate zone, operated side, showing central chromatolysis and eccentrically placed nucleus (Nissl). × 225.

FIG. 8.—Anterior horn cell, operated side, showing typical early "retrogade" cell changes (Nissl). × 260.

*To illustrate Paper by Kahr and Sheehan.*

sympathetic cord or splanchnic nerve. Thus, from an anatomical standpoint, Kiss's view does not appear to differ in any way from those of Kuré, except that Kiss wishes to substitute the name "sympathetic" for "parasympathetic." His reason for this change does not appear clear, for the preganglionic sympathetic fibres are, as generally accepted, confined to the thoracic and upper lumbar regions, whereas the efferent fibres in posterior roots have been demonstrated by Kuré to exist throughout the length of the spinal cord, i.e., also in the cervical lower lumbar and sacral regions.

In reviewing the literature, it is seen that many investigators have been able to establish the presence of fine axons in the proximal stumps of severed posterior roots (Sherrington, Ranson, Kuré, Gagel and Tower). The question still remains undecided whether these axons can be considered as true efferent fibres, persisting because their trophic centres are situated in the spinal cord, or whether, as Ranson and Tower suggest, they are regenerating fibres growing back into the degenerated stump of the posterior root. It is to this aspect of the problem that our attention has been particularly directed.

## METHOD.

If efferent fibres with a trophic centre in the spinal cord exist in the posterior root, then after section of the root between its emergence from the cord and the spinal ganglion, intact fibres in the proximal stump should be demonstrable, after an appropriate interval of time for degeneration of the afferent fibres. The time allotted for degeneration is important. Sherrington, Ranson and Tower were all able to demonstrate intact fibres in the central stumps but believed that they might possibly be regenerated fibres. Extirpation of the ganglion does not completely remove all possible source of regeneration, because of the technical difficulty of successfully performing posterior rhizotomy in small animals without injuring some of the superficial (posterior) fibres of the neighbouring anterior root. To circumvent the possibility of regeneration occurring in the posterior root from the minor but unavoidable injury to the anterior root, we have studied the majority of our cases at a period prior to the onset of regeneration, and yet sufficiently long to allow for the degeneration of the afferent fibres to occur. Since it is extremely difficult arbitrarily to state an exact interval of time after which regeneration may occur, we have used intervals of fifty-four days for myelinated, and twenty-four days for unmyelinated fibres (Ranson, 1929) as periods before which no considerable degree of regeneration can be expected.

Our material consisted of a series of ten cats. In seven of these a laminectomy was performed in the lower thoracic and upper lumbar region. In each animal two roots were divided extradurally, usually the first and second lumbar, occasionally the last thoracic. In a few of these cases only the posterior root was divided. The anterior root could then be seen lying at a slightly deeper (anterior) plane to the severed posterior root. It is always difficult in such a case to be certain that the most superficially lying fibres of the anterior root have not been implicated. In all the other operations, in order to exclude any possible regeneration from the spinal ganglion, this was completely extirpated, the anterior and posterior roots being cut through completely immediately central to the ganglion. The proximal stump of the severed anterior root was now isolated and completely removed as far as its emergence from the dura. Only the proximal stump of the posterior root was thus left projecting. Thus, because of the short time before study of the material, all possible sources of regeneration were reduced to a minimum. The extradural approach is necessary in cases where it is desirous to excise the spinal ganglion. It gives a sufficiently large proximal root stump to enable a systematic study, and where both anterior and posterior roots are severed there can be no question of posterior root-fibres escaping section.

The seven cats treated in the above manner were allowed to live for periods of 15, 24, 29, 30, 36, 45 and 71 days respectively, and were then killed. The completeness of the operation was in each case confirmed by dissection. This was sometimes rendered difficult by the amount of scar tissue formed, but by careful examination the cut ends of the nerves could be always identified. The lumbar spinal cord with the attached proximal root stumps and with the corresponding normal roots of the opposite side, was then removed, and stained by Bielschowsky and Weigert-Pal methods. The upper divided root was often used for Bielschowsky's method and the lower for Weigert stain. The blocks were then cut transversely to the longitudinal axis of the spinal cord, and serial sections were made.

In the remaining three animals, an intradural approach was used and only the posterior root-fibres were cut. The advantage of this approach lies in the fact that the anterior root-fibres do not come into the field of operation and cannot be implicated in any way. The spinal cord is therefore particularly suited for the study of cellular changes following a purely posterior root section. Further in the intradural operation there is less scar formation and the vessels accompanying the root-fibres can be seen and avoided. Besides, not all posterior roots are accompanied by vessels. The vascular disturbance in the spinal cord is therefore almost negligible.

In these three cats lumbar roots were again selected and two roots in each animal cut. They were allowed to live for fourteen days only; when they were killed the spinal cord was removed and fixed immediately in 70 per cent. alcohol. Serial sections were made and stained by the Nissl method. The distal stumps of the cut posterior roots, together with the spinal ganglion, were stained by Marchi for possible evidence of degenerated myelin sheaths. After so short a time (fourteen days) retrograde degeneration of the afferent fibres demonstrated by Marchi can be reasonably excluded (Van Gehuchten, 1903). The anterior roots were treated similarly by Marchi's method in order to establish the accuracy of the operative technique. An attempt was made by the Marchi method to study the peripheral nerve, and evidence of degenerated posterior root-fibres was sought in the corresponding innervated muscles. This was done to demonstrate whether these fibres traverse the spinal ganglion uninterrupted or not.

## FINDINGS.

In the study of the Weigert and Bielschowsky preparations, certain important features became evident. In the first place, in the extradural operation there is practically always a large amount of scar tissue which obscures and renders very difficult the recognition of the posterior root outside the dura and its identification from the anterior root. The intradural parts of the roots are therefore by far the most favourably suited for study, and can be easily identified. Secondly, the importance of serial sections, for only in these can the presence of nerve-fibres be reliably determined in silver-stained preparations. This may have been a source of error in other investigations.

*Bielschowsky's method.*—In our series of seven cats in which the extradural approach was utilized, a moderate number, and in one case a considerable number, of intact axis-cylinders were demonstrable in the intradural portion of the posterior roots. Transverse and oblique sections in which only a short course of the axis-cylinders could be seen, were not dependable in the early cases, as the presence of degenerating fibres was a possible source of error, but a moderate number of normal, healthy and mature axis cylinders of considerable length was found in each case. These fibres presented no varicosities, end-bulbs or branchings, and in our opinion cannot be considered as regenerating or degenerating.

In our early cases, in the region of the scar enveloping both anterior and posterior roots, we were unable to demonstrate satisfactorily the presence of whorls or loops of regenerating axis cylinders.

A number of investigators have been puzzled by the greater number of intact axis-cylinders in the posterior root extradurally and at its point of exit through the dura, than in the intradural portion and its entrance into the cord. Normally, the posterior root-fibres for the segment emerge from the cord at slightly different levels in small isolated bundles, and only converge to constitute a single compact nerve-root at their exit through the dura. Studies of the normal side reveal the same striking contrast in the apparent number of axis cylinders in the various parts of the posterior root.

In the entrance zone of the posterior root in the spinal cord a number of intact axis cylinders were observed. These could be followed for a considerable length arching in a transverse plane through the white matter immediately dorsal to the posterior horn. They could be often seen in three or more bundles sinking into the base of the grey matter of the posterior horn, the most mesial bundle in close proximity to Clarke's column. We were unable to trace these fibres deeper into the grey matter or laterally as far as the periphery. These fibres had no association with the blood-vessels, as observed by Tower. They were healthy, normal and mature in appearance. They were orderly arranged and in no way differed in course, although their number is less, from similar fibres to be seen in normal preparations. Fibres pursuing an aimless course, as described by Tower, from material studied after much longer intervals and permitting the possibility of considerable regeneration occurring, were not seen. However, it is impossible to state definitely that these normal fibres which we have observed intraspinally are the efferent fibres under discussion. They may, on the one hand, be fibres reaching the segment from other levels, or, on the other hand, may be secondary neurones. If the fibres sinking into the grey matter in the region of Clarke's column have their origin in these cells, then they are not neurones of the second order, for it is well established that the cells of Clarke's column do not send axons in this manner.

At the point of entry of the posterior root into the cord, occasional fibres were seen. They could not be followed very far in the grey matter.

*Weigert's method.* — The presence of degenerating medullated sheaths rendered the Weigert studies less satisfactory. However, the Weigert sections clearly showed a small number of healthy medullated fibres amongst the debris of degenerated myelin. These fibres could be traced in the posterior root occasionally for a moderately long course. The majority of these intact fibres were of medium and small calibre. Numerical studies were rendered impossible because of the obscuring globules of degenerating myelin. Kuré also encountered similar difficulty and confined his study to material from cases which had lived over a longer period.

The Weigert studies were convincing, and coincided with the findings from the Bielschowsky preparation.

*Marchi's method.*—Evidence of Marchi degeneration was found in the posterior root distal to its interruption, and in the posterior root fibres traversing the spinal ganglia. In addition Marchi degeneration was found in the corresponding peripheral nerve, distal to the spinal ganglion, and in nerve bundles in the muscles innervated by the divided posterior roots. The posterior roots, spinal ganglia and peripheral nerves were studied serially both longitudinally and transversely. In longitudinal sections the black globules were in the typical chain-like arrangement. The fibres studied transversely presented partial and complete ring formation of Marchi granules at the site of the myelin sheaths.

Careful studies were made of the anterior roots corresponding to the cut posterior roots. All of these anterior roots were found to be normal.

The Marchi studies were made fourteen days after operation, so that one cannot say with certainty that the maximum degree of Marchi degeneration had been reached. We therefore considered it inadvisable to carry out any numerical studies at the present.

*Nissl's method.*—In the sections of spinal cord stained by the Nissl method no evidence of vascular damage or inflammatory disease could be seen. A slight meningeal proliferation and a moderate glial response in the posterior root entrance zone were observed on the operated side.

In serial sections of levels corresponding to the cut posterior roots, changes typical of retrograde cell reaction were seen in isolated cells of the intermediate zone with the exception of the lateral horn.

However, evidence of an accompanying glial response was lacking. A moderate number of anterior horn cells showed similar changes. These cellular changes were confined to the operated side. It is important to note that the anterior root was in no way exposed or subjected to trauma at the time of operation, and on histological examination with the Marchi method showed intact fibres. No changes were observed in the cells of Clarke's column. Unfortunately the levels one or more segments above the operated roots were not studied. Similarly, no obvious changes were seen in the large cells of the posterior horn.

A relative diminution in the number of cells in the intermediate zone on the operated side as compared with the intact side was observed in certain sections, a point upon which Kuré lays great stress. Such variants are within the range of the normal, and because of this fact only rigid histo-pathological criteria should be applied in the study of this cell group.

## DISCUSSION.

In our material intact fibres have been demonstrated in the proximal stump of posterior roots after their interruption between the cord and spinal ganglion. Ranson and Tower also observed intact fibres in this position but were of the opinion that they were regenerated fibres. The time interval selected in the present work was too short to permit any considerable degree of regeneration. Moreover, our sections revealed normal, healthy and mature fibres. They entered the cord at the root entrance zone and could be followed intraspinally for a short distance. However the fibres we have observed dipping into the posterior horn are possibly axons reaching the segment in question from other levels. Further work is required to determine the exact intraspinal course of the intact fibres demonstrated in the central stumps of the severed posterior roots. That they are efferent fibres possessing a trophic centre within the spinal cord is certain. Marchi studies of the distal stumps fully support this contention. Fourteen days after severance of the posterior roots, a moderate amount of Marchi degeneration was demonstrable in the distal ends. We believe that the changes observed represent Wallerian degeneration. The objection often raised that retrograde Marchi degeneration confuses the issue, we believe not to be applicable in these studies. Van Gehuchten (1903), after extensive work with Marchi degeneration, concluded that retrograde degeneration makes its first appearance twenty days after the experimental lesion. In the present work the roots were cut with sharp scissors with the avoidance of any undue traction or trauma.

An interesting observation was the finding of Marchi degeneration peripheral to the spinal ganglion, extending into the small bundles of nerve-fibres in the correspondingly innervated muscles. Joseph, in his studies on cats, observed the same. This is evidence that in the cat at least some of the fibres in question traverse the spinal ganglion without interruption.

The exact localization of the trophic centre of the efferent fibres in posterior roots presents greater difficulties. It would appear from the previous works of Warrington, Lapinsky, Timasheff, and Gagel, and from the present investigation that, following posterior root section, typical so-called "retrograde" cell reactions are found on the same side in: (*a*) The intermediate zone at the level of section; (*b*) the anterior horn cells at the level of section; (*c*) the cells of Clarke's column at a level one or more segments above the site of section.

Changes in the cells of Clarke's column occur in both sides of the spinal cord.

Since such changes occur in isolated cells and never in groups and the cord histologically presents no evidence of vascular damage, the suggestion that the changes observed are due to a traumatic or anæmic change can be reasonably excluded. The possibility of the anterior root being implicated at the time of operation has been clearly avoided in the present work.

Kuré observed the changes in the intermediate zone, but made no mention of the cell changes in the anterior horn and in the cells of Clarke's column. It appears to us from our observations, and those of others, impossible to accept Kuré's conclusions that the efferent fibres in the posterior roots arise from the cells of the intermediate zone. The localization of the trophic centre for such fibres cannot be established from the evidence available at the present.

An explanation for some of the cell changes observed is offered by Gagel, that of a "trans-neuronal" retrograde change. It is a well-established fact that some of the afferent posterior root-fibres end around the cells of the anterior horn at the same level, and around the cells of Clarke's column in the next higher segments. This appears to lend considerable support to the view of a trans-neuronal (inactivity) retrograde cell change. Histologically we believe that it is difficult to distinguish between acute retrograde and transneuronal cellular changes in our material. It is for this reason that we prefer to leave the exact origin of the efferent posterior root-fibres undecided, while in no way detracting from the accumulated evidence in support of their existence.

## SUMMARY.

(1) In the cat, posterior roots from thoracic 12 to lumbar 2 have been sectioned between the cord and spinal ganglion.

(2) Intact fibres have been demonstrated by the Bielschowsky and Weigert methods in the central ends of the severed posterior roots. These fibres were seen entering the cord and studied intraspinally.

They were normal, mature fibres, and could be considered neither as regenerated nor as degenerating.

(3) Wallerian degeneration was observed in the distal ends of the cut posterior root. This degeneration could also be seen in the nerve peripheral to the spinal ganglion.

(4) The observations made are all in support of the existence of efferent fibres in the posterior roots examined.

(5) Nissl studies of the spinal cord revealed changes in the intermediomesial group of cells and in the anterior horn cells. The localization of the trophic centre for such efferent fibres is rendered impossible by the presence of cellular changes apparently occurring transneuronally.

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# THE METABOLIC COST OF SUSTAINED POSTURES IN NORMAL AND CATATONIC SUBJECTS.

BY J. B. GAYLOR AND G. M. WISHART.

*(From the Institute of Physiology, University of Glasgow.)*

THE metabolic cost of muscular tonus and sustained muscular contractions is still a very unsettled problem. While there seems no doubt that certain invertebrates can maintain powerful tonic contractions of their muscles with little, if any, rise in metabolism, the results with mammalian muscle are much more conflicting.

Information has been sought in the metabolism of decerebrate rigidity. The tonic contraction of decerebrate rigid muscles was found by Bayliss [1] to be associated with some heat production, but with very much less heat than that of a corresponding degree of tetanus. In Roaf's [11] investigations of decerebrate cats, the $CO_2$ production remained unaltered and the $O_2$ consumption showed a negligible diminution when the rigidity was abolished by curare or nerve-section. Later experiments by Dusser de Barenne and Burger [3], on the other hand, showed consistently a higher $O_2$ consumption during the rigidity than after its removal by nerve-section or by ethyl urethane. The last authors further remarked that the increased respiratory exchange was much less during decerebrate rigidity than during phasic movements.

A comparison of the cost of postural and phasic contractions, produced in the leg muscles of cats by special modes of stimulation, was made by Weatherhead [13]. She found that postural contraction increased the resting metabolism by 30 per cent., though in some experiments there was little change. In phasic contractions, the $O_2$ consumption increased by amounts varying from 6 to 56 per cent., and the author states that "regular phasic movements can be carried out with a comparatively low metabolic cost, sometimes (with small movement) indistinguishable from the cost of postural contraction." The general consensus of evidence from all these experiments would appear to be that tonic contractions, while causing some increase in metabolism, are more economical than active movements of the same muscles.

Sustained contractions produced by the injection of tetanus toxin have been investigated by Grafe and Schürer [7]; they found no increase in the energy exchange when a local tetanus was so induced in pigs' muscles.

In the domain of human muscle, information has been sought in the state of increased tone existing naturally in some psychotics, and in the postural contractions frequently producible in them; also in similar conditions produced in normal individuals by hypnotic suggestion.

Grafe [5], in determinations of the basal metabolism in mental diseases, noted that subjects with various types of stupor frequently had a subnormal metabolism, and, since this lowered energy exchange might be present in spite of greatly increased muscular tone, he concluded that tone had little effect on the energy output. In a more recent article, Grafe [6] admits, however, that when tonic contraction is maintained against a load, a metabolic rise is to be expected. Such an increase has been demonstrated by Schill [12] for arm and leg postures in catatonic schizophrenics. Schill's general conclusion is that the static work of these catatonic postures produces the same changes in metabolism, heart-rate, ventilation, and blood-pressure as in normal individuals.

Plaut [10] investigated the metabolism of post-encephalitics in their abnormally stiff sitting posture, and found no difference between their metabolism and that of normal subjects sitting "at ease." When the normals voluntarily assumed a tense sitting posture, the metabolism markedly rose. The same author compared the metabolism of a catatonic patient, who could retain a horizontal position with only head and feet supported for ten minutes, with that of a normal individual endeavouring to imitate the same posture. The normal subject was unable to hold the posture for longer than one minute, but the metabolism was followed during a fifteen-minute recovery period in both. Although the total excess metabolism, including the recovery, was the same in both subjects, the $O_2$ consumption per minute of the normal during the actual posture was four times that of the catatonic subject. While the comparison is obviously unsatisfactory owing to the short duration of the experiment with the normal subject, it is reasonable to suppose that he would have shown a much greater total metabolism if he could have maintained the posture longer. These two experiments, along with her failure to find any increase in metabolism on resisting extension in the limbs of a decerebrate rigid cat, led Plaut to conclude that, under certain conditions of increased muscular tone, static work could be performed without increased $O_2$ consumption.

Increased tone produced by hypnotic suggestion of violent muscular exercise has been investigated by Grafe and Traumann [8]; no decisive increase in metabolism above the resting value was obtained. On the other hand, in Gessler and Hansen's [4] experiments, in which the subject had to maintain the loaded or unloaded arm in an abducted position, a quite marked increase in metabolism was found whether the subject was in the hypnotic condition or not.

Finally, mention may be made of Klemperer and Weissmann's [9] report of a few metabolism determinations in a patient subject to prolonged cataleptic attacks. The basal metabolic rate between seizures was + 10 per cent. to + 19 per cent., with a pulse-rate of 68 to 88; during an attack the metabolism in the recumbent position was + 35 to + 40 per cent. with a pulse-rate of 60; while, with the patient still recumbent, the placing of the limbs in an almost vertical position caused a rise of over 200 per cent., the heart-rate increasing to 120.

The present paper adds to these investigations in human subjects, one on the energy exchange (1) under basal conditions, and (2) during posture, in three patients who could maintain their limbs involuntarily in any posture in which they were set, for periods as long as twenty minutes. Two of these individuals were asylum patients, and the third was under treatment for hysteria in a general hospital. As a comparison, similar estimations were carried out in five normal subjects, who maintained voluntarily, as far as possible, an identical posture.

The following are the clinical details of the three pathological cases:—

J.B., aged 53. Occupation, grocer.

On admission to the Glasgow Western Infirmary the patient told the story of being subject to fits of depression ever since he entered business as a grocer. He had failed in business twenty-five years ago and two and a half years ago. After both failures he suffered from curious seizures during which he lost consciousness for varying periods of time. Each attack was ushered in by headache, but the immediate precursor to an attack was a peculiar sensation in the head; this latter symptom was not always present, so that he was frequently unaware when he was about to have an attack. Apparently at the commencement of an attack there is a generalized trembling of the whole body, following this he lies as if he were asleep and he cannot be roused. After his first business failure the attacks came on at frequent intervals during a period of six months. Since his second failure he has had seizures differing neither in type nor in incidence. There is nothing of note in the history of his general health except that he is subject to asthma in bad weather.

*General examination.*—The patient is an intelligent man. In conversation he shows evidence of having had a good education. Apart from manifestations of depression he cannot be said to have any mental abnormality, he is neither delusional nor hallucinated. He is well nourished: examination of the heart, lungs, abdomen, and urine reveals no gross organic disease.

There is no loss of muscle power, the superficial and deep reflexes are all active. There is a complete hemianæsthesia on the left side. He manifests flexibilitas cerea and is able to maintain bizarre postures without showing fatigue. During his stay in hospital the hemianæsthesia was cured by suggestion.

A. T., aged 24.—This patient was admitted into Hawkhead Mental Hospital in 1931 with a history of mental disturbance lasting only a few weeks. From the first he has been a case of catatonic schizophrenia. The fully developed psychosis was preceded by a feeling of despair. This condition lapsed into stupor with catatonia, in which state he has remained. It is worthy of note that the patient had suffered for some years from septic disease of the nasal sinuses, and although operative treatment had been resorted to on more than one occasion, the condition remained unalleviated. An attempt was made to affect the intractable stupor by the administration of thyroid extract, but without result. The condition of the patient when he was observed by us was as has been indicated above. He was in profound stupor, manifestly catatonic and completely shut off from his environment.

M.I., aged 35.—From his admission to Hawkhead Mental Hospital in 1927 the patient has shown evidences of progressive dementia. At first he was capable of fair mental concentration, and he appeared to take some interest in his environment. Within four months of his admission he became quite schizophrenic, showing little interest in his surroundings and answering questions in monosyllables; within ten months he became negativistic and catatonic. When seen by us he was practically in the same state as that which had developed ten months after his admission to hospital. His previous history seems to indicate that he was of the schizoid type in childhood and in adolescence. When a boy he was impulsive, secret, and reticent. As an employee he was unreliable and minor delinquencies brought him into conflict with police authorities.

## EXPERIMENTAL PROCEDURE.

The metabolism estimations were made by the Douglas-Haldane procedure, all the customary precautions being observed. After an air sample had been collected under strictly basal conditions, the patient, still lying on the bed, was placed in the following posture: left arm and fore-arm in line and projecting vertically upward from the shoulder, the wrist being flexed and the hand lying approximately horizontally; left thigh flexed to a right angle with abdominal wall, leg bent at knee to form a right angle with thigh, and foot forming a right angle with the leg. The patient was allowed to remain in this posture for as long as could be permitted without risking the curtailment of the second air collection by a collapse of the posture. After the lapse of this period, which unfortunately could only be a few minutes in duration, the second air sample was collected. In addition to the data required for the metabolism determination, observations were made of the pulse-rate and systolic and diastolic pressures. These records were taken from the arm which was not elevated. The procedure with the normal subjects was identical.

## RESULTS.

Table I gives the original metabolic data for the abnormal subjects, along with the averages for each subject in (1) basal and (2) postural state. Table II shows the same thing for the normal subjects. The

TABLE I.

| Subject | | | Ventilation litres/min. | R.Q | $O_2$ per min. c.c. | Metabolism/Sq.M /Hr. Calories |
|---|---|---|---|---|---|---|
| J. B. .. | BASAL | | 6.14 | 0·91 | 181 | 32 6 |
| | | | 5·15 | 0·86 | 184 | 32·8 |
| | | | 4·84 | 0·85 | 178 | 31·7 |
| | | Average | 5·38 | 0·87 | 181 | 32·4 |
| | POSTURAL | | 7·27 | 0·81 | 281 | 49·4 |
| | | | 8·00 | 0 88 | 278 | 49·8 |
| | | | 7·58 | 0·87 | 274 | 49 0 |
| | | Average | 7·62 | 0·85 | 278 | 49·4 |
| A. T. .. | BASAL | | 3·18 | 0·73 | 193 | 32·3 |
| | | | 3·60 | 0·78 | 182 | 30·4 |
| | | | 2·63 | 0·72 | 177 | 29·2 |
| | | | 2·80 | 0·81 | 165 | 27·8 |
| | | Average | 3·05 | 0·76 | 179 | 29·9 |
| | POSTURAL | | 4 52 | 0 79 | 240 | 40·6 |
| | | | 5·26 | 0 83 | 238 | 39·3 |
| | | | 4·62 | 0·83 | 231 | 39·1 |
| | | | 5·61 | 0·92 | 238 | 40·9 |
| | | Average | 5·00 | 0·84 | 237 | 40·0 |
| M. I. .. | BASAL | | 8·66 | 0 92 | 256 | 48·5 |
| | | | 5·77 | 0·80 | 239 | 44·2 |
| | | | 5·17 | 0·82 | 267 | 49·6 |
| | | | 5·46 | 0·88 | 269 | 50·5 |
| | | Average | 6 26 | 0·85 | 258 | 48·2 |
| | POSTURAL | | 7·45 | 0·77 | 376 | 69·2 |
| | | | 7·00 | 0·76 | 344 | 63·1 |
| | | | 6·67 | 0·79 | 379 | 70·0 |
| | | | 6·75 | 0·88 | 338 | 63 6 |
| | | Average | 6·97 | 0 80 | 359 | 66·5 |

TABLE II.

| Subject | | | Ventilation litres/min. | R.Q. | $O_2$ per min. c.c. | Metabolism/Sq. M./Hr. Calories |
|---|---|---|---|---|---|---|
| G. M. W. .. | BASAL | | 5·04 | 0·81 | 205 | 31·8 |
| | | | 4·91 | 0·79 | 202 | 31·1 |
| | | | 6·05 | 0·82 | 207 | 32·2 |
| | | Average | 5·33 | 0·81 | 205 | 31·7 |
| | POSTURAL | | 8·50 | 0·86 | 353 | 55·3 |
| | | | 8·36 | 0·87 | 345 | 54·1 |
| | | | 9·09 | 0·83 | 361 | 56·2 |
| | | Average | 8·65 | 0·85 | 353 | 55·2 |
| J. B. G. .. | BASAL | | 4·60 | 0·88 | 215 | 36·2 |
| | | | 4·05 | 0·82 | 210 | 35·0 |
| | | | 4·45 | 0·85 | 214 | 36·0 |
| | | | 4·46 | 0·80 | 220 | 36·6 |
| | | Average | 4·39 | 0·84 | 215 | 35·9 |
| | POSTURAL | | 7·06 | 0·90 | 313 | 52·9 |
| | | | 5·84 | 0·80 | 314 | 52·5 |
| | | | 6·36 | 0·86 | 300 | 50·5 |
| | | | 7·22 | 0·85 | 338 | 56·7 |
| | | Average | 6·62 | 0·85 | 316 | 53·1 |
| T. O. .. | BASAL | | 4·95 | 0·73 | 278 | 43·3 |
| | POSTURAL | | 8·05 | 0·78 | 425 | 66·9 |
| J. B. B. .. | BASAL | | 5.47 | 0 85 | 257 | 38·3 |
| | | | 5·70 | 0·90 | 259 | 38·8 |
| | | Average | 5·59 | 0·87 | 258 | 38·6 |
| | POSTURAL | | 7·28 | 0·80 | 384 | 56·8 |
| | | | 6·54 | 0·76 | 376 | 55·0 |
| | | Average | 6 91 | 0 78 | 380 | 55·9 |
| J. W. C. .. | BASAL | | 5·23 | 0·79 | 212 | 35·1 |
| | | | 5·28 | 0·83 | 216 | 36·1 |
| | | | 4·58 | 0·81 | 205 | 34·1 [1] |
| | | | 4·54 | 0·79 | 202 | 33·5 |
| | | Average | 4·91 | 0·81 | 209 | 34·7 |
| | POSTURAL | | 6·69 | 0·76 | 322 | 53·0 |
| | | | 6·14 | 0 77 | 297 | 4·90 |
| | | | 5·91 | 0·79 | 281 | 46·6 [1] |
| | | | 5·72 | 0·76 | 300 | 49·5 |
| | | Average | 6·12 | 0·77 | 300 | 49·5 |

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[1] This pair of determinations after one week's daily practice at maintaining the posture.

third table gives the percentage rise or fall of each factor between basal and postural conditions for each subject, as calculated from the averages shown in Tables I and II. Table IV gives percentage differences calculated in the same way for the circulatory data; to save space, the original data, which in themselves were of no particular interest, are omitted.

TABLE III.

PER CENT. DIFFERENCES $\left(\frac{\text{Postural–Basal}}{\text{Basal}} \times 100\right)$

| Subject | Ventilation | R.Q. | $O_2$ per min. | Metabolism/Sq.M./Hr. |
|---|---|---|---|---|
| J. B. .. .. | + 41·4 | − 2·3 | + 53·5 | + 52·5 |
| A. T. .. .. | + 63·8 | + 10·5 | + 32·5 | + 33·8 |
| M. I. .. .. | + 11·4 | − 5·9 | + 39·0 | + 37·8 |
| Average per subject | + 38·9 | + 0·8 | + 41·7 | + 41·4 |
| G. M. W. .. | + 62·0 | + 4·9 | + 72·2 | + 74·1 |
| J. B. G. .. .. | + 51·0 | + 1·2 | + 47 0 | + 48·2 |
| T. C. .. .. | + 62·5 | + 6·8 | + 52·8 | + 54·5 |
| J. B. B. .. .. | + 23·6 | − 10·3 | + 47·0 | + 44·8 |
| J. W. C. .. .. | + 24·6 | − 4·9 | + 43·5 | + 42·7 |
| Average per. subject | + 44·7 | − 0·5 | + 52·5 | + 52·9 |

TABLE IV.

PER CENT. DIFFERENCES $\left(\frac{\text{Postural–Basal}}{\text{Basal}} \times 100\right)$

| Subject | Pulse-rate | Systolic | Diastolic | Pulse-pressure |
|---|---|---|---|---|
| J. B. .. .. | + 20·7 | + 18·5 | + 13·4 | + 28·4 |
| A. T. .. .. | + 2·0 | + 3·4 | + 5·9 | − 0·8 |
| M. I. .. .. | − 0·9 | + 6·1 | + 6·5 | + 5·3 |
| Average per subject | + 7·3 | + 9·3 | + 8·6 | + 11·0 |
| G. M. W. .. | + 21·1 | + 15·5 | + 18·2 | + 9·1 |
| J. B. G. .. .. | + 20·0 | + 16·6 | + 22·7 | + 6.2 |
| T. C. .. .. | + 33·3 | + 17·4 | + 13 9 | + 25·0 |
| J. B. B. .. .. | + 15·1 | + 15·7 | + 28·1 | − 5·3 |
| J. W. C. .. .. | + 15 6 | + 13·6 | + 20 6 | 0 0 |
| Average per subject | + 21 0 | + 15·8 | + 20·7 | + 7·0 |

## DISCUSSION OF RESULTS.

We make little comment on the absolute values of the basal metabolism of the three patients. These were graded according to the mental condition of the subjects. A. T., in whom there was marked stupor, was decidedly subnormal; J. B., who was depressed and lethargic but not stuporous, was less so; while M. I., who mumbled continuously and incoherently, was decidedly hypernormal. The increased metabolic rate of M. I. was no doubt largely an expression of his continuous state of excitement but partly also due to the muscular movements involved in his continuous mumbling.

Of more interest are the metabolic changes during the maintenance of the posture. There is no doubt that, in the pathological cases, ventilation, oxygen consumption and metabolism all show a decided rise; the R.Q. shows a negligible change.

Comparing these changes with those obtained in the normal subjects, in the latter the R.Q. is again unaffected, but the percentage alterations in the other three data are distinctly higher. This higher percentage rise in the metabolism of the normals is due in part to the weighting of the average by the high results of G. M. W.; if his results were neglected, the rises in normal and pathological subjects would be much closer. At the same time, it might equally be argued that the average rise per subject would, in the abnormals, have been lower if the influence of J. B., the most normal of the pathological cases, were removed.

There is much to be said for considering J. B. in a different category from the other two patients. Clinically, J. B. was a case of hysteria, with long periods of remission during which he was a perfectly normal individual; experimentally also, the postural disturbance in this subject of both metabolism and cardiovascular system resembled that of our normal controls. At the same time, he possessed the faculty of maintaining postures apparently involuntarily and without strain for periods much longer than was possible with any normal individual; in view of this, and in view of our ignorance of the mechanism of these sustained postures and of whether the mechanism is identical in the different psychoses, we have thought it wiser to consider all the abnormal subjects as a single group. Adhering to this basis of a simple division into abnormal and normal subjects, the posture is maintained at a cost approximately one-fifth less in the psychotics. If, however, J. B.'s results are excluded, and comparison is made only between the two catatonics and the normals, the economy of cost of the posture in the pathological cases is still more pronounced, even when the high results of G. M. W. are neglected.

One cause for the increased cost in the normals is seen in the data of Table IV. The pulse-rate, systolic pressure, and diastolic pressure are all much less disturbed in the patients than in the healthy subjects; in fact, if again the results of J. B. are excluded from the pathological series, the circulatory disturbance in the remaining two subjects is very small indeed. The increased heart work which evidently accompanies the posture in the normals must contribute in some measure to the higher metabolic cost, but its entire responsibility for the difference between catatonic and normal seems rather doubtful.

The further question arises as to whether the absence of circulatory disturbance in the two catatonics can be taken to indicate a difference of mechanism between their postures and those of the normals. This assumption, however, cannot be made too hastily, since we can hardly be certain that, during the maintenance of a particular posture, exactly the same amount of muscle is involved in the schizophrenic as in the normal person.

From the psychiatric point of view it is clear that in schizophrenia there is a great dissociation between the afferent and efferent sides of the psyche. In a normal subject the maintenance of a fixed posture gives rise to a bombardment of the sensorium by stimuli from the tonically fixed musculature: this is attended by a feeling of discomfort which, in turn, finds expression through efferent neurones to cause rigidity in muscles other than those concerned primarily with the maintenance of the particular posture. As confirmatory of this phenomenon, we recollect the subjective experience of discomfort which we felt first in the muscles directly involved, and then in the muscles which became rigid as a result of this primary discomfort. We are very doubtful if this phenomenon occurs to any degree in the catatonic schizophrenic. If these people do not react to painful stimuli, they cannot be expected to react to stimuli coming from muscle maintaining a specific posture. The result of such a psychic anæsthesia would naturally be that more muscle is involved in the maintenance of posture in the normal individual than in the schizophrenic. As the findings indicate, the more schizophrenic the individual is, the more economically does he maintain cataleptic posture.

Three further points are of interest. First, there are many references in the literature to the close correlation between pulse-rate and metabolism, not only in health but in various pathological states in which both are disturbed, e.g., hyperthyroidism, leukæmia, etc. In the data obtained from the two catatonics, we have the exceptional instance of an average increase of metabolism of 30 to 40 per cent. with an average rise in pulse-rate of only half a beat per minute.

Secondly, in the circulatory data of the normal subjects the rise in diastolic pressure during posture is a striking feature, being greater than the rise in systolic. A similar behaviour has been commented on by Cathcart, Bedale, and McCallum [2] and by others in experiments on voluntary static work. This behaviour is simply explained by the venous stasis associated with the sustained muscular contraction. Accepting this explanation, the absence of an equal stasis in the catatonic is very puzzling.

Thirdly, the possible effect of practice in diminishing the postural metabolism was considered, and one of our subjects (J. W. C.) practised the maintenance of the posture for about fifteen minutes daily throughout a week. A determination at the end of the week showed that neither metabolic (see Table II) nor circulatory disturbances had diminished.

## SUMMARY.

Determinations of the energy exchange were carried out, (1) under basal conditions, and (2) during posture, in three psychotic patients who could involuntarily maintain any posture in which they were set. The results were compared with those of five normal subjects imitating the same posture.

A definite increase of metabolism during the posture was observed in both normal and pathological cases.

On average, the metabolic cost of the posture was about one-fifth greater in the normals than in the psychotics.

The circulatory disturbance due to the posture was considerably greater in the normals.

It is a pleasure to acknowledge our indebtedness to Dr. James H. MacDonald, of Hawkhead Mental Hospital, and to Dr. John Gracie, of Glasgow Western Infirmary, for allowing us free access to patients under their charge. We are also indebted to Professor E. P. Cathcart for his interest in the investigation.

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# THE TESTIS AND REFERRED PAIN.

BY H. H. WOOLLARD,
*Department of Anatomy, St. Bartholomew's Hospital Medical School, London,*
AND
E. ARNOLD CARMICHAEL,[1]
*Research Unit, National Hospital, Queen Square, London.*

THE subject of referred pain has been so frequently discussed in recent times that there is no need to present any elaborate introduction to it.

The investigations of Head resulted in the formulation of certain conclusions which have never been quite accepted by other investigators and most have modified them in some way or other. Head [3], adopting the conception of referred pain, proceeded to define the position of the reference on the surface of the body of pain, the occasion of which was some pathological change in a viscus, and he compared these places of reference with those of the cutaneous areas of the segments of the body which he had already mapped out in other studies. He observed that the referred pain did not usually occupy the whole of the cutaneous area of the segment but commonly was concentrated in a small part which was called the maximal point. Further, he observed that many viscera, such as the heart, stomach, uterus, &c., gave rise to referred pains which occupied widely separate segments. Such observations, together with the conclusion that in general neither the cervical nor the lower lumbar segments were the seat of referred pains from viscera, led to the hypothesis that the sympathetic efferent outflow was accompanied by an afferent sensory inflow, restricted approximately to the same region of the spinal cord.

The segmental relations of this viscero-sensory inflow provide therefore the anatomical basis upon which the referred pain was explained. This basis has been challenged by several investigators. Some have denied that the viscera ever refer their sensations, while others assert that even if they are sensitive they do not refer their pains but vaguely localize them somewhere near the mid-line of the body.

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[1] Work undertaken on behalf of the Medical Research Council

Carrying the argument further, it is asserted that the ability to refer sensations is a function of somatic nerves only, and that these refer the sensations dependent on their deeper branches to fibres innervating the surface areas of the body. Others have accepted the possibility of reference from viscero-sensory nerves under special conditions, the most important of which has been the presence of an adequate stimulus.

Recently we [5] published some observations on the results of stimulating the central end of the divided phrenic nerve. The object of these investigations was to observe the position of any pain the patient might experience when the central end of the cut phrenic nerve was pinched, and secondly to observe any modification in this pain when the area in which it was felt had been rendered anæsthetic by a local injection of novocain. We found that pain was invariably aroused by stimulation of the central end of the phrenic nerve, and it was felt by the patient as though concentrated in a small area just below and internal to the acromio-clavicular joint of the same side. The position was constant in each patient and varied but slightly between one patient and another. Infiltration of this area with novocain made no difference to the intensity or the position of the pain. We concluded from these investigations that the idea of referred pain was a valid one, that it depended on events taking place in the central nervous system and that it was not annulled by anæsthetizing the skin area in which it was felt as had been claimed; further, that the diaphragm behaved as a viscus in that the sensations aroused from it were referred to a distant area.

These experiments were criticized by Morley [4] and Loyal Davis [2] on two grounds. In the first place, it was objected that the peripheral area of anæsthesia was not extensive enough and that the pain was therefore not abolished. This objection is groundless since we induced areas of cutaneous anæsthesia four or more inches in diameter, and we infiltrated not only the superficial but also the deeper tissues. The pain was referred right into the area which was anæsthetic.

To meet the second objection, that the diaphragm could not properly be compared to a viscus since it is innervated by a somatic nerve, the following observations on the testis were made.

It had occurred to us that the testis might be regarded as a proper viscus and one suitable upon which observations in regard to referred pain might be made. It is accessible to investigation; its migration from within the abdomen to its scrotal position occasions wide differences in the segments from which it and its coverings might draw their nerve supply, and it has of course the same relation to peritoneum as a viscus lying within the abdomen. It was hoped that the different positions of the various nerves which reach it might permit of them being blocked by local anæsthetics and thus enable us to study what happens under such conditions when the testis was stimulated.

Theoretically at any rate it could be postulated that sensory nerves might reach the testis from several sources. These might be: (1) Through afferent nerves accompanying the internal spermatic artery along with the sympathetic fibres; (2) or by sensory nerves coming from the hypogastric plexus along the vas; (3) from the ilio-inguinal nerve; (4) from the genital branch of the genito-femoral nerve; and (5) by way of the posterior scrotal nerves.

Cushing [1] had already reported that in operations upon inguinal hernia division or blocking of the genital branch of the genito-femoral rendered a hernial sac, the structures of the cord and the testis itself insensitive to handling, cutting and ligation, i.e., in this respect the testis behaves like the gut.

It was decided that one of us would act as the subject and the other as observer and the attempt be made to block these nerves by local injection and observe the results of stimulation of the testis.

After some preliminary experimentation the method adopted of stimulating the testis was as follows: the testis was drawn forwards in the scrotal sac and supported by fingers placed below it. A scale pan was rested on the testis and weights placed in this compressed the testis and epididymis between the supporting fingers and the scale pan. Known weights were placed in the pan and left there till the subject described what sensations he experienced and where he felt them. The injections were made with 4 per cent. novocain and 1 in 60,000 adrenalin and were made for the most part by Mr. R. E. Norrish, to whom our thanks are due.

The following results were obtained after injection of the posterior scrotal nerves, the injection being carried out by infiltrating along the posterior attached margin of the scrotum as far as the middle line. Anæsthesia was obtained over one half of the scrotum. The anæsthesia did not extend on to the thigh nor over the pubes, but included a triangular area on the body of the penis along its ventral surface, the base below and the apex half-way along the shaft.

*Experiment* 1.—The left testicle (posterior scrotal nerves blocked and the scrotum of that side anæsthetic).

| Stimulus | Response |
|---|---|
| 300 grm. | Slight discomfort in the left groin. |
| 350 ,, | More discomfort in the left groin but no testicular sensation. |
| 400 ,, | These produced similar responses to 350 grm. |
| 450 ,, | |
| 500 ,, | |
| 550 ,, | |
| 600 ,, | Definite pain in the left groin. |
| 200 ,, | No sensation. |
| 300 ,, | Very doubtful sensation. |
| 350 ,, | Slight discomfort in the left groin. |
| 400 ,, | Indefinite discomfort in the left groin. |
| 450 ,, | |
| 500 ,, | |
| 600 ,, | Slightly more definite discomfort. |
| 650 ,, | Very definite discomfort in the left groin. |
| 850 ,, | Definite discomfort in the left groin. |
| 1,000 ,, | Severe pain in the left groin without discomfort appreciated in the testis itself. |

### OBSERVATIONS ON THE RIGHT TESTICLE.

| | |
|---|---|
| 300 grm. | Slight discomfort in the right groin. |
| 350 ,, | More discomfort in the right groin. |
| 400 ,, | As the previous but some discomfort in the testis. |
| 450 ,, | Discomfort in both inguinal regions. |
| 500 ,, | Discomfort in the region of the external abdominal ring extending into the testis. Discomfort on the right side in the groin as well. |
| 550 ,, | Severe pain on the inner side of the right thigh with indefinite testicular sensation. |
| 600 ,, | Definite testicular pain followed by a dull ache in the right lumbar region dorsally. |
| 650 ,, | Severe testicular pain on the right side |

From these observations we drew the conclusion that in the absence of the scrotal nerves, the source of the sensory supply of the scrotal tissues, compression of the testis gave rise, not to pain in the testis, but to pain referred to the inguinal canal region in the territory of the first lumbar segment.

*Experiment* 2.—A second experiment was made of injecting the posterior scrotal nerves along the posterior attachment of the scrotum on the left side. Sensation was abolished over the left half of the scrotum and the ventral aspect of the shaft of the penis towards its attachment. Plucking and pinching of the skin as well as pin-prick revealed no sensation in the coverings of the testis.

### RIGHT TESTICLE.

| Stimulus | Response |
|---|---|
| 50 grm. | No pain. |
| 100 ,, | ,, ,, |
| 200 ,, | ,, ,, |
| 250 ,, | ,, ,, |
| 300 ,, | Uncomfortable feeling in the right testis. |
| 200 ,, | No pain. |
| 350 ,, | ,, ,, |
| 400 ,, | Uncomfortable feeling in the right testis. |
| 500 ,, | Discomfort in the right testis |
| 525 ,, | ,, ,, ,, ,, |
| 625 ,, | Uncomfortable feeling in the right testis. |
| 725 ,, | Definite pain in the right testis. |

### Left Testicle.

| | |
|---|---|
| 200 grm. | No sensation. |
| 400 ,, | Indefinite discomfort in the left groin |
| 500 ,, | Dull ache in the left groin. |
| 450 ,, | Discomfort in the left groin. |
| 200 ,, | No sensation. |
| 400 ,, | Indefinite discomfort in the left groin. |
| 300 ,, | No sensation. |
| 425 ,, | Discomfort in the left groin. |
| 525 ,, | Definite discomfort in the left groin. |
| 625 ,, | Definite ache in the left groin. |
| 725 ,, | ,, ,, ,, |

In this experiment the scale pan was removed entirely between each test. This proved to be a considerable improvement in the method of conducting the experiment, as the subject was able to interpret more clearly the effect of the application of different weights.

Digital compression produced no testicular sensation.

A re-testing of the right testicle, which had not had the posterior scrotal nerves injected, gave at 500 grm. a painful sensation felt as though it arose in the testicle itself.

Thus we concluded that when posterior scrotal nerves are blocked sensation is not felt in the testis but referred to the groin, approximately over the internal abdominal ring in the first lumbar segment.

*Experiment* 3.—An injection was made along the attachment of the scrotum in the region of the external abdominal ring. This produced an anæsthesia of the left anterior part of the scrotum and of the adjacent inner part of the thigh. The cremasteric reflexes were present on both sides.

### Left Testicle.

| Stimulus | Response |
|---|---|
| 200 grm. | Mild discomfort in the testis. |
| 300 ,, | ,, ,, ,, ,, |
| 500 ,, | Discomfort in the testis. |
| 550 ,, | Pain in the testis. |
| 400 ,, | Discomfort in the testis. |
| 300 ,, | Very mild discomfort. |

### Right Testicle.

| | |
|---|---|
| 200 grm. | No definite sensation. |
| 400 ,, | Discomfort in the testis. |
| 500 ,, | Pain in the testis. |
| 200 ,, | No discomfort. |
| 450 ,, | Pain in the testis. |

This anæsthesia which affected branches of the ilio-inguinal was without effect on sensation aroused in the testis.

*Experiment* 4.—Injection of the left posterior scrotal nerves as in previous experiments. Anæsthesia complete over one-half of the scrotum and part of the penis.

LEFT TESTICLE.

| Stimulus | Response |
|---|---|
| 200 grm. | No sensation. |
| 500 ,, | Discomfort above the middle of Poupart's ligament. |
| 300 ,, | Discomfort in the left groin. |
| 200 ,, | No sensation. |
| 450 ,, | Discomfort in the left groin. |
| 825 ,, | Severe discomfort in the left groin. |

RIGHT TESTICLE.

| Stimulus | Response |
|---|---|
| 825 grm. | Pain in the testicle (it was noted that the subject exclaimed "That is quite different from the left side.") |

The cremasteric reflexes were present on both sides and an attempt was made to abolish this reflex. Novocain and adrenalin were then injected into the neck of the scrotum, the cord being pushed well away. The dartos became somewhat contracted and the left cremasteric reflex was abolished. It was hoped that the sensory fibres with the sympathetic, which we assume to be present, had escaped, but apart from the results of the experiment no way of proving this was available to us.

LEFT TESTICLE.

| Stimulus | Response |
|---|---|
| 200 grm. | No sensation. |
| 400 ,, | ,, |
| 500 ,, | ,, |
| 600 ,, | ,, |
| 850 ,, | Vague sensation in the abdomen. |
| 825 ,, | Vague sensation in the abdomen but not possible to say where. |

*Experiment* 5.—The posterior scrotal nerve and the ilio-inguinal nerve were injected and an attempt was made to inject the genito-femoral. The finger was inserted as far as possible into the external ring and the cord pushed to one side and then the needle was inserted through the aponeurosis of the external oblique and 1·5 c.c. of 2 per cent. novocain was injected along with 1 in 60,000 adrenalin. When the injections were completed there was anæsthesia of the left half of the scrotum, part of the shaft of the penis and of the inner side of the thigh. The cremasteric reflex was almost completely abolished; it was possible to elicit, however, a slight contraction of some fibres near the external ring, but those passing down the scrotum and around the testis did not respond.

RIGHT TESTICLE.

| Stimulus | Response |
|---|---|
| 50 grm. | Sensation of contact. |
| 285 ,, | Discomfort in the testis. |
| 300 ,, | Slight pain in the testis. |
| 250 ,, | Discomfort in the testis. |
| 300 ,, | Pain in the testis. |
| 200 ,, | Slight discomfort in the testis. |
| 400 ,, | Pain in the testis. |
| 350 ,, | ,, ,, ,, |

Left Testicle.

| | |
|---|---|
| 200 grm. | No sensation. |
| 450 ,, | Vague sensation in the abdomen above Poupart's ligament. |
| 500 ,, | Ache on a level with and just internal to anterior superior spine of the ilium. |
| 650 ,, | Ache reproduced in same place as previous test. |
| 400 ,, | No sensation. |
| 700 ,, | Dull ache was felt as though in the upper pole of the testis and also in the lumbar region dorsally. |
| 900 ,, | Dull ache as though at the upper pole of the testis. |
| 450 ,, | No sensation. |
| 900 ,, | Dull ache felt as if it might be in the upper pole of the testis and also experienced dorsally in the back. |

Right Testicle.

| | |
|---|---|
| 900 grm. | Pain felt at once in the testis. |

No other weights were applied to the right testicle during this experiment.

In this last experiment (Experiment 5) two kinds of responses were elicited. A reference of a dull aching character was obtained in the abdomen, the maximal points being situated in the anterior and posterior regions of the tenth thoracic segment. Secondly, the subject also replied that he felt a dull ache as though it was in the upper pole of the testis. It is to be remarked that the first pain experienced was referred to the abdomen and back, and the later tests produced the sensation of the dull aching in the upper pole of the testicle.

The nature of the experiments made it extremely difficult for us to decide to what extent the local injection had blocked the various nerves. We had every reason to believe that the posterior scrotal and the ilio-inguinal nerves were completely blocked. The fact that a few of the upper fibres of the cremaster muscle responded reflexly indicated that at least some fibres of the genito-femoral nerve had escaped being blocked by the novocain. The earlier experiments showed that the presence of the genito-femoral and the absence of the posterior scrotal produced a characteristic response with a constant reference to the first lumbar segment at a stimulus threshold of about 500 grm.

Since these features do not occur in the present experiment, and since there was abolition of reflex contraction of the cremaster except for a few of its higher muscular loops, we are inclined to the opinion that the responses obtained from the subject do not depend on the escape of some fibres of the genito-femoral nerve from the action of the anæsthetic.

This leads to the supposition that both the referred pain in the tenth dorsal segment and the pain described as though it were situated in the upper pole of the testis depended on the presence of afferent fibres mingled with the sympathetic fibres reaching the testis. These sensory fibres would then, when sufficiently stimulated, be the basis upon which pain would be at the same time localized to the organ from which the impulses start, and also be the occasion of its reference to the segmental area of the cord with which these fibres are connected.

We felt we could not further resolve this problem by the method we had chosen and that we must turn to suitable clinical cases. This we thought we could now do more profitably since we had determined the kind of stimulus which would be efficient, the different thresholds of stimulation which would excite the various groups of sensory fibres and had obtained evidence of the functional contribution to sensation which superficial, deep and visceral sensory nerves gave.

When comparison of the various thresholds for pain is made, it is found that in the intact testis pain may be aroused with a pressure equal to 200 to 300 grm., but if the posterior scrotals are anæsthetized the threshold is raised to the region of 500 grm. When the ilio-inguinal and genito-femoral nerves are also blocked, the stimulus necessary to produce a definite pain is raised to the neighbourhood of 800 grm.

The location of the referred pains in these experiments fully confirms the work of Head [3]. In the experiment with the posterior scrotals alone blocked, pain is referred to the region of the external abdominal ring, which is the territory recognized as the maximal point of reference of the first lumbar segment; as the genito-femoral nerve, derived from the first and second lumbar segments, is functioning, the pathway for this reference is apparent. Again the reference to the abdominal wall anteriorly and the lumbar region posteriorly, following anæsthetization of all the nerves except those fibres travelling along the spermatic artery, depends on the evolution of the testis from the tenth dorsal segment with its consequent segmental nerve supply.

It was hoped that these experiments could be made more illuminating by applying the results to clinical cases, and it has been our good fortune to examine two cases of crush fracture of the spinal column which substantiates our experimental work.

(1) C. T., aged 35, had a crush fracture of his spinal column which resulted in a complete motor palsy of both legs, with a total loss of sensation to all forms of superficial and deep pain, temperature, touch, vibrations, &c., up to the lower level of the tenth segment on both sides of the body.

Testicular sensation was tested as had been done in our previous experiments. The scrotum was completely anæsthetic and analgesic.

At no time during the experiment did the patient feel a sensation in the region of the testicle or groin. When these tests were repeated, using digital pressure, he first felt a sensation which he referred to a spot about half-way between the umbilicus and the anterior superior iliac spine on the same side; when digital pressure was increased, he commenced to have pain in the mid-lumbar region on the same side. Both these points corresponded with the maximal points of reference of the tenth dorsal segment.

Right Testicle.

| Stimulus | Response |
|---|---|
| 400 grm. | No response. |
| 600 ,, | ,, |
| 700 ,, | Very faint sensation in the back on the right side in mid-lumbar region. |
| 900 ,, | The sensation is more definite. |
| 1,000 ,, | Very definite pain in the mid-lumbar region, pain is of a sickening character. |

Left Testicle.

| Stimulus | Response |
|---|---|
| 400 grm. | No response. |
| 700 ,, | ,, |
| 900 ,, | Feels an ache in the left mid-lumbar region. |
| 1,000 ,, | Sensation is very definite with characteristics similar to the experiment on the right side. |

Severe handling of the epididymis and rolling of the spermatic cord between the fingers failed to produce any sensation. When the spermatic cord was pulled he complained of a vague sensation in the abdomen.

In this case the anæsthesia demonstrated that from and including segment D.11 caudally there was no connection between the peripheral pathways for sensation and the cerebrum. Segment D.10 was however intact. It seems thus justifiable to assume that the impulses which he appreciated and referred had to enter at the level of the tenth dorsal segment or above it: this would therefore exclude the posterior scrotals, the ilio-inguinal and the genito-femoral as being the pathway and leaves open only an afferent pathway along the spermatic artery, entering the cord at the tenth dorsal segment.

(2) In the second case, again a crush fracture, anæsthesia was complete up to the lower level of the first lumbar segment on the right side and of the ninth dorsal segment on the left side. There was also on the left side a complete absence of a cutaneous flare to scratching over the last three dorsal segments, with wasting of the lower half of the left rectus abdominalis, affording evidence that the peripheral pathway for sensation had been injured in these segments.

In this second case, though the patient stated that the pain on the right side was in the testicle, he pointed to the region of the groin; we feel it legitimate to assume that the pain which he felt was actually localized to the region of the inguinal canal, in the sensory domain of the first lumbar segment. In favour of this is the fact that the threshold of the stimulus of the definite pain was in the region of 500 grm., a similar figure to that obtained in our early experiments with the posterior scrotals anæsthetized. When the stimulus was increased to the region of 1,000 grm. the pain was not only appreciated in the first lumbar segment, but also in the tenth dorsal segment: this result is again a replica of the threshold level we obtained in our personal experiments.

Tests for testicular sensation in this case gave as follows:—

RIGHT TESTICLE.

| Stimulus | Response |
|---|---|
| 200 grm. | *Nil.* |
| 300 ,, | Something in the right testicle (pointed to the groin). |
| 400 ,, | Something in the right testicle. |
| 500 ,, | Very definite sensation in the right testicle (pointed to the groin). |
| 600 ,, | Very definite sensation in the right testicle (pointed to the groin). |
| 700 ,, | Pain in the right testicle (pointed to the groin), with an ache in the abdomen too vague to localize. |
| 800 ,, | As in 700. |
| 900 ,, | As in 800. |
| 1,000 ,, | Pain in the right testicle (pointed to the groin), with a pain below and to the right of the umbilicus and also in the right lumbar region (at the maximal points of reference in tenth dorsal segment). |

LEFT TESTICLE.

Weight up to 1,500 grm. failed to be appreciated in any way whatsoever.

On the left side no pain was appreciated whatsoever in the testicle. As the level of anæsthesia included the tenth dorsal segment, it is fair to assume, in conjunction with our other observations, that pain impulses from the testis do not enter the cord at a higher level than the tenth dorsal segment.

These observations, therefore, on clinical material uphold our conclusions drawn from the experiments on ourselves.

## SUMMARY.

(1) A series of experiments by means of nerve block have been carried out to determine the pathway of painful sensation from the testis. These experiments have been amplified by observation on clinical material.

(2) In the absence of the posterior scrotal nerves pain is no longer localized to the testis but to the maximal points of reference in sensory segmental areas.

(3) With the genito-femoral nerve intact, pain is referred from the testis to the maximal points of the first lumbar segment.

(4) The posterior scrotal and genito-femoral nerves being rendered

insensitive, pain from the testis is appreciated in the tenth dorsal segment and is localized to the side stimulated.

(5) The threshold for the arousing of pain at these situations differs; it is 300 grm. for the reference of pain to the testicle, 500 grm. to the first lumbar segment, and 800 grm. or more to the tenth dorsal segment.

(6) Reference may be obtained from the testicles when the only pathway for sensory impulses is by way of the fibres surrounding the spermatic artery and thus reference is independent of a somatic nerve supply.

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# SYRINGOMYELIC COMPLICATIONS OF SPINA BIFIDA.

FRANK A. TURNBULL.
*Vancouver, B.C.*

SPINA BIFIDA is an uncommon condition, and syndromes relative to its various clinical phases are necessarily ill-defined. Between such widely separated extremes as that of severe spinal malformation with exposure of the central canal, and that of spina bifida occulta with only a slight deficiency in the vertebral laminæ, lies a variegated group of cases. This large intermediate group is usually classified on a pathological basis, according to the degree of closure of the spinal cord, meninges and spinal column. The majority of recent contributions to the subject have dealt chiefly with operative technique, and have naturally focused interest on the gross topographical relationships. Less careful scrutiny has been made of the clinical groups into which certain of the more obscure cases fall.

One such group displays a clinical picture simulating syringomyelia. Although cases of this type cannot be very unusual, a survey of the literature reveals few reports and very meagre pathological data. The following case is presented to illustrate the clinical progress of these lesions, and to draw attention to certain difficulties in diagnosis:—

J. H., male, aged 30, was admitted to the National Hospital, Queen Square, on November 2, 1932, under the care of Dr. Gordon Holmes. He complained of pains in his left leg of two years' duration, unsteady gait for one and a half years, and weakness and awkwardness of his arms for three months.

He had been a premature infant, and at birth had a pedunculated tumour on the back of his neck This tumour, which was about the size of a hen's egg, was removed when he was aged 1 year. The attending doctor reported to the parents that the growth had a pedicle, the base of which was too deep for removal He believed that this pedicle was connected with the spinal cord. From infancy the patient had weakness of his right hand and arm He was never able to perform fine movements with his right hand, although he could use it for eating.

He had always stooped slightly, and this tendency had become more marked during the few years before admission. In 1930 he began to suffer intermittently from dull pains in his left leg. They were most troublesome during periods of overwork. The pains seemed to involve the muscles of his left thigh, and to a less extent his left calf, and were associated with a feeling of stiffness. They recurred at intervals varying from a few weeks to a few months. In 1930 he also first became aware of some difficulty in appreciating the temperature of water with the left leg when in a bath.

During the summer of 1931 he noticed that his gait was occasionally unsteady, and he began to stumble frequently. At about the same time he complained of weakness of his left arm and aggravation of the existing weakness of his right arm. In the autumn of that year he was still able to do a five-mile walk, although he tired more readily than formerly. After Christmas, 1931, he noticed occasional involuntary jumping movements of his right arm. These movements returned during the week before admission.

In January, 1932, he started to have attacks of urinary frequency, lasting one or two days and recurring about every two weeks. This trouble became gradually worse during the year. In the last nine months he had incontinence of urine on about six occasions.

About March, 1932, he found great difficulty in raising himself from a supine position. This symptom became gradually more marked. During the last three months the weakness of his right arm became more pronounced, and he noticed extreme awkwardness in its use. He also found that his left grip was weaker. This condition of his arms remained about the same. Two months before admission walking became more difficult. His legs, particularly the left, would occasionally give way beneath him.

*Condition on admission.*—He was very intelligent and mentally alert. His head appeared to have sunken forward on to his chest. His lips were slightly cyanotic. He spoke well, but with some effort. He seemed to have difficulty in regulating his breathing during conversation, and occasionally had to give a quick gasp. There was an infrequent, rapid and jerky movement of his right fore-arm.

*The cranial nerves* were normal, apart from a moderately marked Horner's syndrome on the right side. The anterior muscles of his neck were unduly prominent. There was good power of extension of the head, but power of flexion was feeble.

*Upper limbs.*—The right hand was held with the wrist slightly flexed and all the fingers and the thumb extended, while the left hand showed a slight tendency to claw deformity. The right arm was slightly spastic. There was complete atrophy of the levator anguli scapuli and teres muscles on both sides, and of the right trapezius muscle. Only a few fibres represented both rhomboids, infraspinati and the left trapezius. The muscles of both upper arms were wasted and very weak, while the muscles of the fore-arms and the intrinsic muscles of both hands were slightly wasted and moderately weak. All the muscles of the right arm were slightly weaker than the corresponding muscles of the left arm. The finger-to-nose test was performed very poorly on both sides. It was quite impossible to touch fingers to thumb with the right hand, but this was fairly well performed on the left. No fibrillation of muscles was noted.

*Trunk.*—He could not sit up in bed without assistance, and was only able to get out of bed by rolling and twisting to the edge. There was very little expansion of the chest on attempting to take a deep breath, and there was complete paralysis of the right side of the diaphragm. This was confirmed by X-ray screening. The erector spinæ muscles of his lower back were moderately weak.

*Lower limbs.*—There was rather poor muscular development, but no actual wasting. Both lower limbs showed a slight increase of tone. The extensors of both thighs and the dorsiflexors of the left foot were slightly weak, but all other muscle-groups of the legs showed fairly good power. Co-ordination in the heel-to-knee test was very poor on both sides.

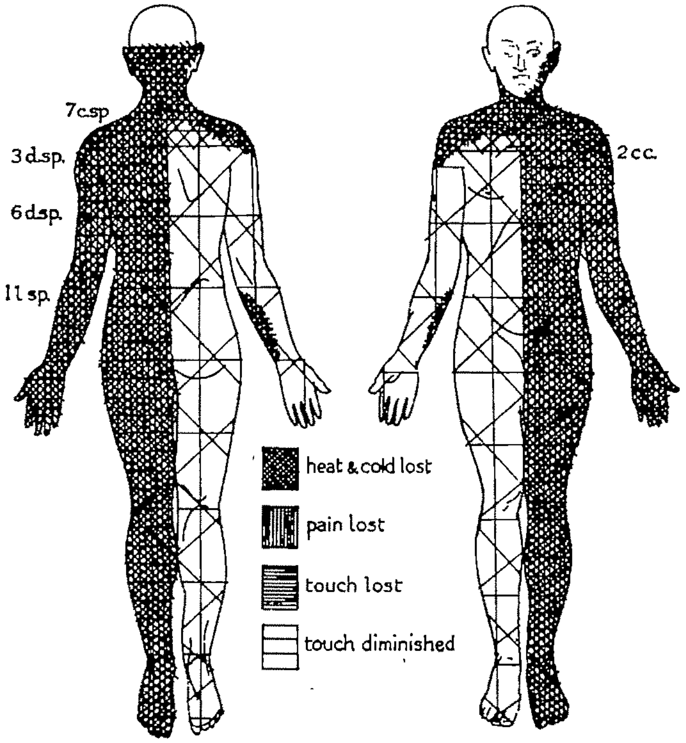

FIG. 1.

*Reflexes.*—The biceps, triceps and supinator jerks were present and normal in the left arm, and in addition there was a slight but definite finger-jerk. These reflexes were all present in the right arm, and all except the triceps-jerks were exaggerated on that side. The abdominal reflexes were absent. The knee-jerks and ankle-jerks were present and normal. Plantar stimulation caused extension of the great toes on both sides.

*Sensation* (see fig. 1). There was complete loss of the sensations of light, touch, pain, heat and cold around the neck and over the upper surfaces of the shoulder-girdle. This loss of sensation extended up over the angle of the jaw and the lower half of the external ear on the left side. Below the level of complete anæsthesia on the left side there was complete loss of the sensations of pain, heat and cold, and the sensation of light touch was moderately diminished. On the opposite side there was a similar loss of sensation over a small area on the ulnar border of the fore-arm, but over the rest of this side all forms of superficial sensation were only slightly diminished (fig. 1). Appreciation of vibration was absent in the fingers of the right hand, and over both patellæ and shins. The sense of position was lost in the fingers of the right hand, present in the fingers of the left hand, and absent in both great toes. Sense of passive movement was completely lost in the right arm, present in the left arm, slightly diminished in the right leg, and moderately diminished in the left leg.

*Spine.*—He had a marked kyphosis of the cervico-dorsal spine, the greatest angle being in the region of the first dorsal vertebra. Movements in the kyphotic area were greatly restricted. There was a mid-line scar extending from just below the external occipital protuberance to over the fifth cervical spine. This scar was sunken into the nape of the neck, giving the impression that there was little depth to the musculo-ligamentous covering of the spine in this area. The spinous processes of the second, third and fourth cervical vertebræ seemed to be missing.

Radiographs showed some deficiency of the spinous processes and laminæ of the second, third, and to a lesser degree of the fourth cervical vertebræ.

*Gait.*—His gait was slow and shuffling, with an associated wobbly tremor of his whole body. His head was held very rigidly and the arms did not swing freely.

*Other systems.*—The only other evidence of congenital anomaly was a very highly arched palate. The blood Wassermann was negative. Lumbar puncture revealed an initial pressure of 272 mm. of water, a rapid rise on jugular compression to over 300 mm., and a rapid fall back to 265 mm. on release of pressure. After the removal of 5 c.c. of fluid the pressure was 200 mm. The fluid was clear, with no cells, a negative Pandy test, total protein of 0·02 per cent. and a negative Wassermann.

An operation was performed on November 25, by the late Sir Percy Sargent, because of the rapid extension of the paralysis. Under gas-oxygen and ether anæsthesia the laminæ of the upper six cervical vertebræ were exposed. A conical-shaped projection of dura was found to extend dorsalwards through the aperture in the laminæ of the third and fourth cervical vertebræ. Its apex merged into the dense fibrous tissue of the old mid-line scar. When this dural sac was opened it appeared to be lined with greatly thickened arachnoid, from the inside of which many fibrous bands extended down to the dorsal surface of the spinal cord. The lumen extended dorsally to the apex of the sac and was apparently continuous with the subarachnoid space. The cord was not enlarged and over its dorsal aspect in the exposed area it appeared quite normal. The fibrous bands were divided about 1 cm. above the cord, and the stalk of the meningeal protrusion was removed.

Progress after the operation was very stormy, characterized chiefly by respiratory distress. He expired on November 27.

Autopsy: Permission was obtained for examination of the spinal cord only.

*Gross appearance.*—Nothing abnormal was noted except over the dorsal aspect of the cervical cord at the operative site. The arachnoid for several segments above and below the centre of this area appeared to be considerably thickened. The dorsalward extension of the thickened arachnoid had been cut off about 5 mm. above the surface of the cord. The dorsal roots were unaffected.

*Microscopical examination.*—Nothing abnormal was found in the pons at the level of the seventh cranial nerve nucleus, nor in the upper end of the medulla. At the level of the caudal extremity of the inferior olive the ventral spino-cerebellar tract showed some demyelination, but otherwise the section was normal.

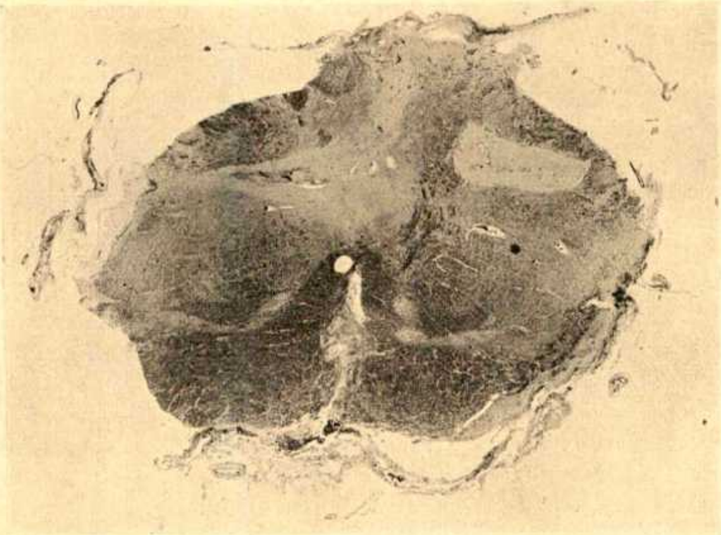

FIG. 2.—Medulla oblongata. Section at the upper end of the pyramidal decussation Note the demyelinated areas around the masses of fibrous tissue in the upper quadrants of the section.

At the level of the upper end of the pyramidal decussation there were on either side, ventral to the dorsal column nuclei, short oblique bands of dense fibrous tissue surrounded by an oval area of degenerated tissue. The latter area was completely demyelinated. The area of degeneration cut across the sensory decussation and involved the site of the dorsal nucleus of the vagus on one side (fig. 2).

At the level of the lower end of the pyramidal decussation there was some fibrous tissue thickening of the walls of capillaries in the columns of Goll. Oblique bands of fibrous tissue were seen in the same relative position as at the higher level. The area of demyelination was slightly more extensive and involved most of the columns of Goll.

At the level of the first cervical segment the pia-arachnoid was moderately thickened. There was a narrow marginal area of demyelinated parenchymal tissue around the dorsal two-thirds of the circumference of the cord. Blood-vessels throughout the dorsal columns showed very marked fibrous thickening of their walls. The anterior horn cells were slightly deficient on one side.

At the level of the upper half of the second cervical segment the thickening of the pia-arachnoid was increased, particularly over the dorsal surface. In the lower half of this segment (fig. 3) a dorsal mid-line fissure appeared, which extended down to, but did not enter, the ependymal canal. The latter was enlarged and triangular in outline. Thickening of the membranes of the cord was very marked. Dense bands of fibrous tissue extended down into the dorsal fissure. Scattered through the fibrous tissue over the dorsum of the cord were small round and oval areas of tissue which appeared identical with the spinal parenchyma. They were unmyelinated, and with Mallory's phosphotungstic-acid-hæmatoxylin stain appeared to be composed entirely of densely packed neuroglial fibres. Extending almost the whole length of one dorsal horn was a thick band of fibrous tissue which enclosed two irregular narrow fissures. The anterior horn cells on the opposite side were almost entirely missing. There was an area of degenerated parenchymal tissue in the region of both lateral horns.

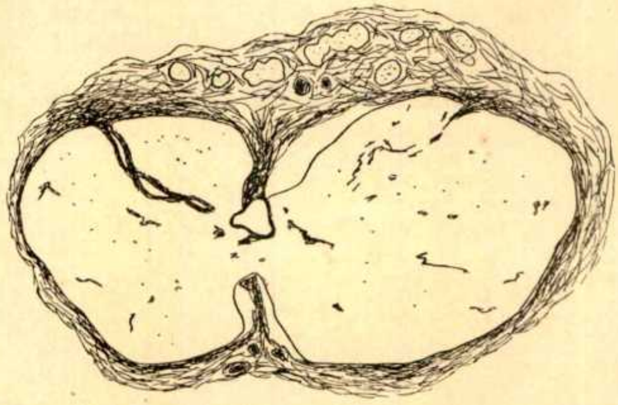

FIG. 3.—Lower end of second cervical segment. Note the enlarged central canal, the dorsal fissure, the fissure in one posterior horn, and the islands of neural tissue in the mass of fibrous tissue above the cord.

Serial sections were made of a block consisting of the third and fourth cervical segments. In the upper sections of the third cervical segment the dorsal fissure was closed, but the central canal was still widened. The thickening of pia-arachnoid was very marked around the whole cord, and the dorsal mass of fibrous tissue contained the same "islands" of neural tissue. The marginal band of demyelinated tissue was still present, and at this level

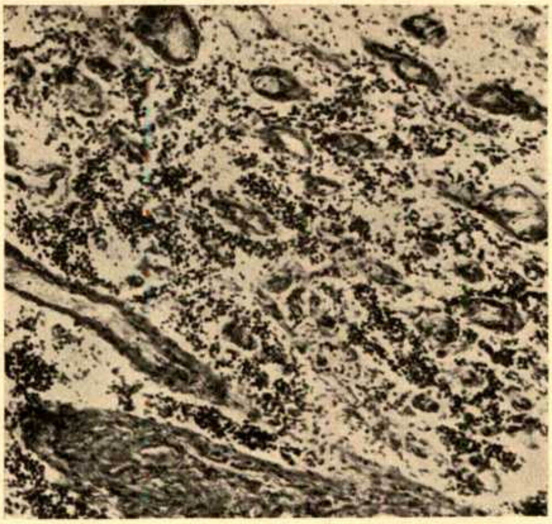

FIG. 4.—Area of neoplastic infiltration in the anterior horn region of the third cervical segment. Van Gieson × 175.

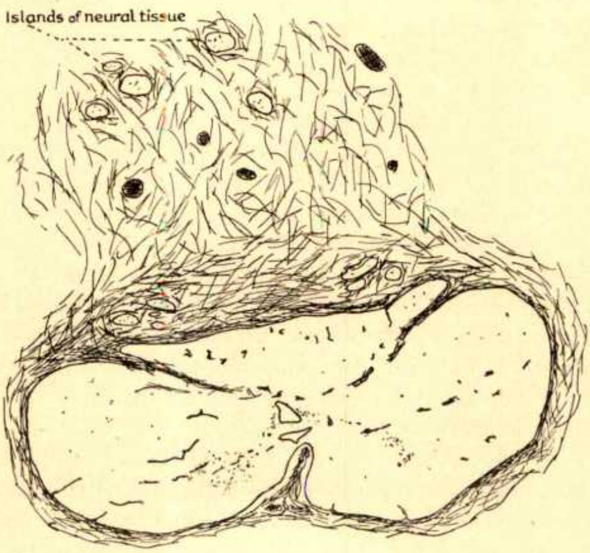

FIG. 5.—Lower end of third cervical segment. Note the islands of neural tissue in the fibrous mass above the cord.

was about one-third the depth of the anterior fissure; this condition was found down to the fifth cervical segment. The anterior horn of one side was devoid of nerve cells, while the other anterior horn showed only a few nerve cells.

Scattered throughout the regions of the anterior horn and extending to the anterior margin of the cord were thickly scattered small round nuclei which were dark staining and had eccentric nucleoli; the surrounding cytoplasm was moderate in amount. The nuclei were arranged in a pseudo-rosette manner in a few areas, but on the whole were irregularly dispersed throughout the parenchymal tissue. There was a narrow clear zone around most of the blood-vessels. The affected area was exceedingly vascular, and the blood-vessels all showed marked fibrous thickening of their walls. Very few mitotic figures were noted (fig. 4). The infiltrated area spared only the direct pyramidal tract zone in the anterior third of the cord, and was entirely devoid of myelin.

At the level of the lower half of the third cervical segment (fig. 5) the dorsal extension of fibrous tissue was at its greatest depth. The islands of neural tissue appeared further away from the dorsal surface of the cord, some of them being at the most dorsal margin of the section. There were no anterior horn cells and in the anterior third of the cord there appeared the same dense infiltration of small round cells and thickened capillaries as was described above. Near the centre of one anterior horn there was a small irregular cavity lined with degenerated glial cells.

Descending the block by sections it was noted that the anterior horn cells gradually reappeared on one side in the fourth cervical segment, but did not reappear on the other side until the fifth cervical segment. The islands of neural tissue in the dorsal extension of fibrous tissue gradually approached closer to the dorsum of the cord (fig. 6).

At the level of the middle of the fourth cervical segment the islands of neural tissue had coalesced in the fibrous mass above the cord. As at the higher level they were completely unmyelinated, and Bielschowsky's stain demonstrated absence of axis-cylinders in these areas. They were separated from the dorsal columns of the cord by a wide shallow cavity which extended from one dorsal root entry-zone to the other. This cavity was lined by fibrous tissue which merged laterally with the dense fibrous tissue of the thickened pia-arachnoid. The central canal was small and round, but immediately dorsal to the canal another irregular cavity lined by degenerated glial tissue had appeared. There was moderate infiltration by small round cells in the central canal area and in the region of one posterior horn, as well as in both anterior horns.

At the level of the lower end of the fourth cervical segment (fig. 7) five cavities were apparent in the cord. The wide horizontal fissure was unchanged. The central canal was still small. There was a narrow fissure in both posterior horns lined by dense fibrous tissue, and a narrow slit running laterally between one posterior and anterior horn which was lined by degenerated glial cells.

At the level of the upper end of the fifth cervical segment (fig. 8) the dorsal horizontal fissure did not extend from side to side, but appeared to be

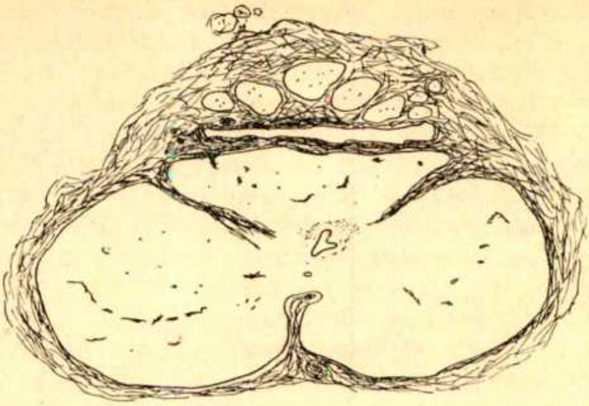

FIG. 6.

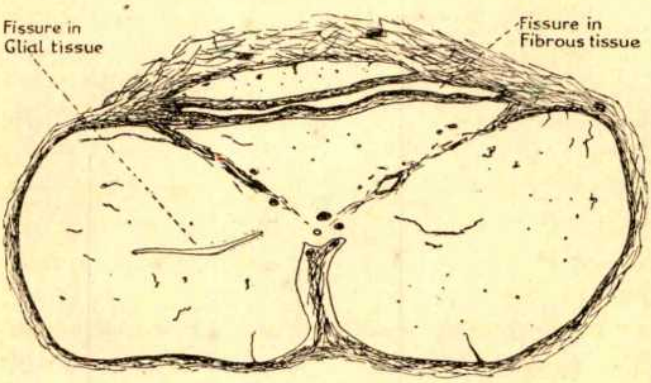

FIG. 7.

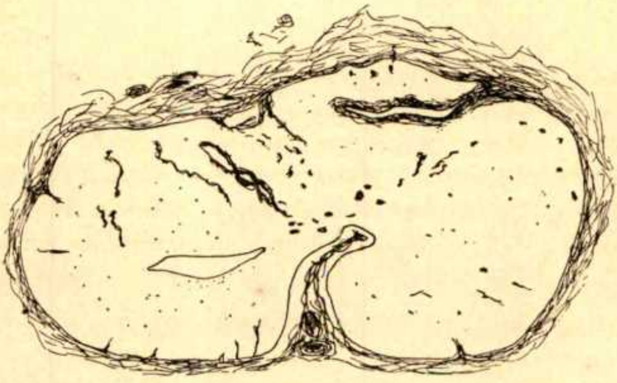

FIG. 8.

FIGS. 6, 7 and 8.—Sections of the spinal cord at the levels of the 4th and 5th cervical segments, showing the formation of the neural "islands" by the splitting off of the dorsal surface of the cord. Other fissures and fibrous tissue septa are seen in the region of the dorsal horns and between the dorsal and ventral horns on one side.

formed by an invagination of fibrous tissue from the point of entry of one posterior root. It extended about two-thirds of the way across the cord. In this section there was also a small crescentic fissure in one anterior horn, lined by degenerated glial tissue. At the lower end of this segment the central canal was normal. There were short irregular fibrous septa in the posterior horns and the posterior columns. The pia-arachnoid was moderately thickened.

At the level of the sixth and seventh cervical segments a thick band of fibrous tissue extended into one posterior horn. There was a very narrow marginal zone of demyelination over the dorsal two-thirds of the cord, and slight demyelination of the lateral pyramidal tracts. At the level of the eighth cervical segment there was a very small fissure lined with fibrous tissue in one posterior horn. At the level of the first dorsal segment this fissure had become much longer but remained narrow, and there was obliteration by fibrous tissue of the root-entry zone. The central canal was wide and shallow. At the level of the fourth dorsal segment the fissure in the posterior horn had become very narrow. The cord below this level was normal.

## COMMENT.

This patient was completely incapacitated by an advancing lesion of the spinal cord. Loss of all forms of sensation over the neck and upper part of the shoulder-girdle indicated an extensive lesion of either the posterior roots or of the posterior horns in the upper cervical region of the cord. There was evidence of damage to the pyramidal tracts as well, particularly on the right side, and to the anterior horn cells or anterior roots from the second to the fifth cervical segments. The degree of distal loss of sensation, and the absence of any severe pains in the distribution of the cervical nerves, was thought to argue against a root lesion. There was presumably a diffuse lesion extending over several segments of the cord, affecting the anterior and posterior horns, the posterior columns to a slight extent, and the pyramidal and antero-lateral tracts on one side severely and on the other side moderately. The patient's age, and the history of slow onset with early appearance of loss of thermal sensation, lent weight to the possibility that a large syringomyelic cavity in the cord was the cause of all his disability. The incipient signs of respiratory failure showed that early demise was certain unless some relief could be afforded. Whether there was any reasonable hope for benefit from surgery was a debatable point.

The appearance at the operation verified the history of meningo-myelocele, but provided no clue to the nature of the intramedullary lesion. Examination of serial sections of the cord was necessary before the latter condition could be appreciated.

Partial failure in closure of the embryonic medullary groove initiated the disease, and was indirectly responsible for all the subsequent pathological changes. The most important of these developments was the process which resulted in the formation of multiple syringomyelic cavities. In addition there appears to have been a progressive disturbance in the blood supply of part of the cervical cord. A third factor, the importance of which it was difficult to estimate, was the appearance of a small amount of neoplastic tissue at the site of greatest disturbance of the cord.

The fibrous-tissue septum which stretched between the tips of the posterior horns in the fourth cervical segment separated the dorsal columns from the functionless neural tissue dorsal to the cord. This tissue was composed of densely packed neuroglial fibres and was devoid of myelin and axis-cylinders. It probably represented remnants of the primitive dorsal roof-plate which had failed to migrate from the neural tube during the formation of the dorsal roots. This neuroglial mass extended into the fibrous tissue which constituted the core of the meningeal protrusion.

An analogous condition in a child of 7 months was described by Barker [1] in 1904. In this case there was a cystic protrusion of dura between the spines of the first and third dorsal vertebræ. The arachnoid and a stalk of neural tissue merged into the translucent wall of this cyst. The neural element appeared to arise from the columns of Goll. It was widest near the cord, and gradually tapered off as it approached the inner wall of the meningeal protrusion. The arrangement of the posterior roots was not altered. Barker presumed that the narrow stalk contained a potential canal communicating with the central canal of the spinal cord.

No apparent neurological disturbance had resulted in my case from the short oblique bands of fibrous tissue in the caudal end of the medulla. Their microscopical appearance suggested that syringomyelic cavities would soon have appeared in that region. Similar dense bands of fibrous tissue in the posterior horns of the upper cervical segments accounted for the complete anæsthesia over the neck and shoulder-girdle. The fissures which were noted in several sections of these posterior horns would have caused few, if any, additional signs. Most of these fissures were mere shallow slits which involved very short sections of the cord. The dilated central canal in the lower end of the second cervical segment involved less than one segment.

The development of the terminal illness was hastened by progressive disturbance in the blood-supply of the cervical cord. The dorsal root element which was incompletely split away from the cord during fœtal development was nourished by part of the arterial supply destined for the posterior and lateral surfaces of the cord. The posterior root arteries, which provide for this area, do not anastomose to any great extent with each other, and the postero-lateral plexus which they form is relatively independent of the anterior arterial plexus. Portions of the cervical spinal cord, particularly the dorso-lateral areas, probably received only a bare substinence of blood with no alternative collateral supply at the time of birth. Following severance of the stalk of the meningocele at the age of one year there resulted a dense scar uniting the posterior tissues of the neck with the protruding sac of dura and arachnoid. Under these conditions any movement of the neck would have caused some traction on the pia-arachnoid with temporary embarrassment of circulation in the small blood-vessels. In later life progressive kyphosis of the lower cervical and upper dorsal spine further increased the amount of traction on the thickened pia-arachnoid. It was significant that increase in his kyphosis coincided with the onset of the major symptoms of spinal cord disease.

The cellular infiltration of the anterior third of the cord in the third and fourth cervical segments was neoplastic. This area of infiltration was limited to the parenchyma of the cord, and was extremely vascular. It resembled most closely the type of tumour classified by Roussy and Oberling as ependymoglioma. The anterior horn cells had entirely disappeared in this area. At higher levels of the cord where there was no neoplastic tissue the anterior horn cells were greatly diminished in number, so that any clinical significance of the tumour was open to question.

The intramedullary cavities which may form in cases of spina bifida are typical in every respect, according to Henneberg [2], of true syringomyelia. These cavities may be of connective-tissue vascular type which behaves like an inflammatory process, or may arise from a primary gliosis with disintegration. Henneberg made a very complete pathological study of a case of spina bifida in an infant, in which there was found an incomplete closure of the laminæ of the tenth dorsal to the coccygeal vertebræ and characteristic syringomyelic cavities in the middle and lower dorsal segments of the cord. Here, as in our case, a few of the cavities were lined by degenerated glial cells, but the majority by fibrous tissue.

Klippel and Feil [3] have described the only adult case in the literature in which post-mortem findings were available. The history corresponded very closely to that of our case. The patient was a man aged 60. There had been some atrophy and weakness of one arm and of the ipsilateral leg which dated from birth. Very slight deformity of the affected hand had become apparent at the age of 35. At the age of 58 muscular weakness began to advance rapidly and involve the other arm. Within a year he became unable to walk. Examination revealed bilateral atrophy of the tongue, atrophy of the muscles of one arm, signs of pyramidal tract affection, and a dissociated anæsthesia of the hand and of the ipsilateral leg and foot. There was a palpable depression in the mid-line of the spine in the lower sacral region (spina bifida). Post-mortem examination disclosed an irregular syringomyelic cavity extending over the greater part of the cord, which communicated with the ependymal canal and also with gutter-shaped depressions on the dorsum of the cord.

Seven cases [4, 5, 6, 7, 8, 9] of spina bifida occulta cervicalis, in which an additional diagnosis of intramedullary fissure of the spinal cord has been made, have been reported, but none of these has had post-mortem verification. In only one of this group [4] was the fully developed syndrome of syringomyelia present. In the other cases there was clinical evidence of an isolated intramedullary lesion, and this was surmised to be a syringomyelic fissure because of the associated spina bifida.

The symptomatology of these cases of syringomyelia combined with spina bifida has been described by Klippel and Feil as the "hydromyelic, ependymal and arachnoid syndrome." Attaching a name to a syndrome of such rarity is of doubtful value, but may serve to recall their pathology when intramedullary lesions of the cord are suspected in the presence of spinal malformation.

## SUMMARY.

A case of cervical spina bifida is reported, in which there developed in early adult life signs suggesting a syringomyelic lesion of the cord.

Operation disclosed the stalk of a meningocele, but no gross deformity of the spinal cord.

Post-mortem examination of the spinal cord showed: (*a*) multiple small syringomyelic cavities; (*b*) fibrous-tissue thickening of the pia-arachnoid and of the walls of blood-vessels in the cord; (*c*) a stalk of functionless neural tissue extending from the dorsum of the cord into the lining of the meningeal protrusion; (*d*) a primitive ependymal tumour, which was of doubtful clinical significance.

The author wishes to express his thanks to Dr. Gordon Holmes for permission to publish this case, and to Dr. J. G. Greenfield for his assistance in the preparation of post-mortem material.

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# IPSILATERAL REPRESENTATION IN THE MOTOR AND PREMOTOR CORTEX OF MONKEYS.[1]

BY PAUL C. BUOY,[2] M.D.

AND

JOHN F. FULTON, M.D.

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IN studying the electrical excitability of the motor and premotor areas in monkeys [4], well-marked responses of the ipsilateral extremities were repeatedly observed on stimulating near the superior precentral sulcus, and subsequent histological examination [4, 5] has indicated that the excitable region lies for the most part in the premotor area of the cortex. A careful analysis has accordingly been made of the locus of the ipsilateral response, the character of the movement which it evokes, and the course of the nervous pathways involved. The present paper contains a full description of the results obtained.

Similar ipsilateral movements have been observed incidentally by other workers, but a thorough analysis of the phenomenon has not previously been undertaken. A review of relevant literature will therefore be deferred until the discussion.

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[1] From the Laboratory of Physiology, Yale University School of Medicine.

[2] On leave of absence from the University Clinics, University of Chicago.

## I.—Stimulation Experiments.

Detailed observations have been made on twenty-seven animals, all primates, and unmistakable ipsilateral movements in response to faradic stimulation in the cortex were seen in twenty-one specimens. The species studied were as follows: 21 common macaques (*Macaca mulatta*[1]), 1 Java monkey (*Macaca irus*), 2 baboons (*Papio papio*), 1 gibbon (*Hylobates lar*), and 2 chimpanzees (*Pan satyrus*). In four of these animals no ipsilateral response could be demonstrated and in two it was questionable. The failure to obtain the ipsilateral response in the gibbon, in one chimpanzee and in two of the monkeys, was probably due to the depth of ether anæsthesia, or to the use of the barbiturates as anæsthetics (see below).

### *Technical Procedures.*

The animals were anæsthetized with ether in all cases in which ipsilateral responses were successfully obtained. The cortex was exposed under profound anæsthesia by means of the conventional five-sided bone-flap and during stimulation the anæsthesia was allowed to become somewhat lighter. Full aseptic precautions were generally observed, and the animals were permitted to survive the procedures in order that the results of the ablations mentioned in the second part of this paper might be observed. To facilitate adequate histological examination ablations were carried out by section of the cortex with a sharp knife followed by blunt dissection. The larger vessels were either clipped with silver clips or coagulated with the Davis-Bovie electro-surgical knife [11, Appendix].

Both monopolar and bipolar faradic stimulation was employed with diphasic make and break stimuli, and all the usual precautions were taken against spread of current. When the monopolar electrode was used the diffuse electrode was placed in the rectum. The responses presently to be described were obtained with almost equal ease with each form of stimulation. Galvanic currents were not utilized. When aseptic precautions were observed a DuBois-Reymond inductorium was used and for acute experiments a Harvard inductorium. Intensity of stimulation is expressed in terms of distance of the secondary coil from the primary. In a few experiments the specially controlled method of cortical stimulation described by Dusser de Barenne and Marshall [7] was utilized (see Experiment 5). Cellophane tracings of the chief markings were taken whenever a cerebral hemisphere was exposed, and accurate charts were thus made of all points stimulated [11].

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[1] The nomenclature used is that of the "List of the Vertebrated Animals" of the London Zoological Society, edited by S. S. Flower in 1929 [9] (see Fulton and Zuckerman [13]).

### (1) *Localization of Excitable Area for the Ipsilateral Response.*

In every case in which an ipsilateral response was obtained it was most readily evoked from a sharply circumscribed area lying about the middle of the superior lip of the superior precentral sulcus (fig. 1). With somewhat more intense stimulation, however, the response could be obtained from an area extending 2 to 3 mm. in all directions from this

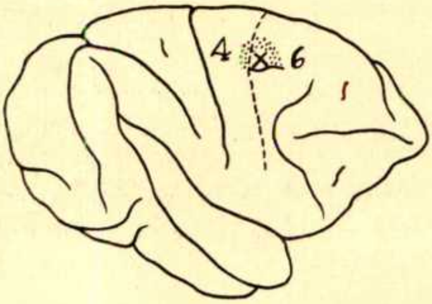

FIG. 1.—Experiment 1. Right cerebral hemisphere, *Macaca mulatta*. Dotted area lying above the superior precentral sulcus is the excitable area for responses in the ipsilateral lower extremity. "X" indicates the most excitable point. The broken line marks the boundary between Area 4 and Area 6 of Brodmann.

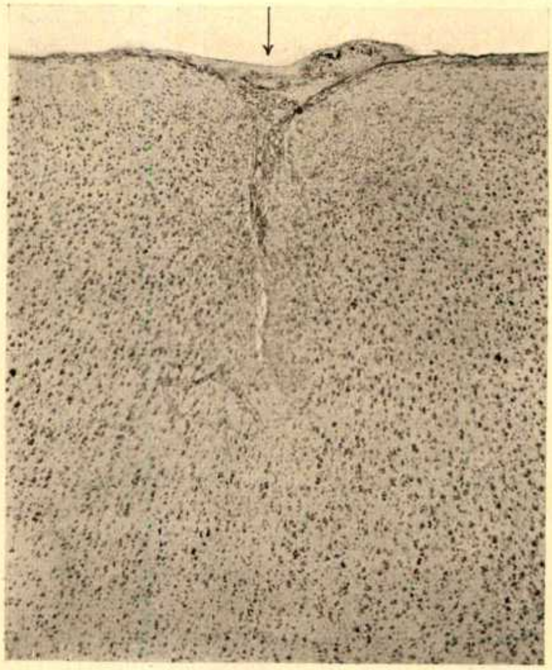

FIG. 2.—A small lesion (↓) was made at the point from which ipsilateral responses were most readily obtained. This section through the lesion shows that it lies in the premotor cortex (Area 6) since there are no Betz cells in the fifth cortical layer. Toluidine Blue (× 50)

central excitable focus. A thorough exploration of the motor and premotor areas has failed to yield any other specific area from which ipsilateral responses can be obtained, but this in itself does not preclude ipsilateral representation being more diffusely present elsewhere in the hemisphere. For convenience of description this specific excitable focus will be termed the " ipsilateral area."

Microscopical examination of the ipsilateral area has indicated that it lies in the premotor region (Area 6 of Brodmann), just anterior to the true motor cortex (Area 4 of Brodmann; see fig. 2).[1] With stronger stimulation the ipsilateral area could be readily extended posteriorly into anterior parts of the motor area (fig. 1). In no instance, however, was the point of maximum excitability for the ipsilateral response found in the motor area itself.

### (2) *Characteristics of the Ipsilateral Response.*

Ipsilateral movement from cortical stimulation was generally seen predominantly in the lower extremity, and in some animals it was entirely restricted to the lower extremity. The movement usually consisted of sustained extension of all joints. This response (in animals with intact spinal cords) was always associated with complex movements of the contralateral lower extremity of the type readily evoked from the premotor cortex [4]. The contralateral movement was ordinarily opposite in sign to the ipsilateral, i.e., flexion at all joints instead of extension, but this was not invariable. Rarely flexion of the ipsilateral lower extremity was observed and this was usually associated with contralateral extension. Other types of response in the ipsilateral lower extremity, such as inversion and eversion, abduction and adduction, have been less commonly seen. In some cases stimulation of the inferior lip of the superior precentral sulcus elicited movement in the ipsilateral upper extremity, usually flexor in character.

The general characteristics of the ipsilateral response are well illustrated by the following experiment:—

*Experiment* 1 (*Area* 6 *series, No.* 2).—*January* 11, 1933: *Exposure left cerebral hemisphere*: *elicitation of usual contralateral responses from Areas* 4 *and* 6, *also ipsilateral response from superior lip of superior precentral sulcus*: *extirpation of Area* 4, *and posterior part of Area* 6.

*February* 6: *Re-exposure left hemisphere*; *extirpation remainder of Area* 6.

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[1] In this paper all designations of cortical areas have reference to Brodmann's [2, 3] well-known architectonic maps of the monkey and anthropoid cortex.

*March* 10: *Exposure of right cerebral hemisphere; elicitation of usual responses from Areas* 4 *and* 6; *extension of the ipsilateral lower extremity on stimulation of superior precentral sulcus*; *Area* 6 *undercut*; *ipsilateral response abolished*; *Area* 4 *still highly excitable.*

The subject of this experiment was a small male monkey (*M. mulatta*) weighing 1,650 grm.

*First operation.*—On January 11, 1933, under ether anæsthesia, the convexity of the left cerebral hemisphere was exposed. The cortex was stimulated using a monoplar electrode, the indifferent electrode being in the rectum. From the motor cortex the usual discrete sustained responses were elicited and the premotor cortex showed its usual excitability. From the superior lip of the precentral sulcus a slow flexion of the ipsilateral lower extremity could be repeatedly obtained. Subsequently a block of cortical tissue, including the motor area and that from which the ipsilateral response was obtained, was extirpated. On microscopic examination it was seen that the ipsilateral response had been elicited from the posterior part of Area 6 (fig. 2).

*Second operation.* On February 6 the left hemisphere was again exposed and the remainder of Area 6 removed.

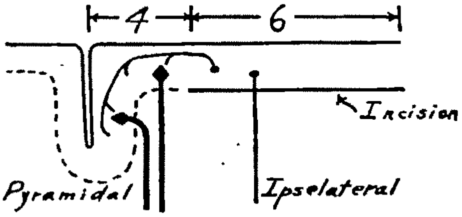

FIG. 3.—Experiment 1. Diagrammatic sketch of the undercutting of Area 6. The incision cutting the ipsilateral pathway, a direct projection from Area 6, leaves intact the trans-cortical fibres from Area 6 to Area 4 which conduct the impulses for the sustained contralateral responses.

*Third operation.* On March 10 the right cerebral hemisphere was exposed. Stimulation of the motor cortex (Area 4) elicited the usual discrete sustained responses at a threshold of 11 cm. with electrodes as before. At 10 cm. the usual complex contralateral movements were obtained from the premotor cortex (Area 6). With stimuli of slightly greater intensity (9·5 cm.), extension of the ipsilateral lower extremity was readily obtained from the superior lip of the superior precentral sulcus and for a short distance above it (fig. 1). These movements could not be obtained from any other part of the exposed cerebral cortex or from stimulation of the dura including the falx cerebri. The ipsilateral response was invariably associated with a complex contralateral movement, usually flexor in character. As usual all responses from the premotor cortex had a longer latency than movements elicited from Area 4, and the latency of the ipsilateral responses was distinctly greater than that of the contralateral.

An incision was then made anterior to Area 6, separating it from the prefrontal cortex (Area 9). This did not affect the excitability of Areas 4 and 6. With a spatula the entire premotor area was undercut (fig. 3), so that its only remaining attachment was with Area 4. Stimulation of Area 6 still evoked the sustained contralateral responses which are elicited by fibres passing to Area 4 [4]. All other responses from Area 6 both contralateral and ipsilateral were completely abolished. However, the excitability of Area 4 remained unchanged.

The block of tissue (Area 6) which had been undercut was now extirpated, and microscopical study showed that the extirpation had extended just posterior to the boundary between Areas 4 and 6 which is indicated in fig. 1. (The results of extirpation in this animal are described below in Experiment VI.)

This experiment, which was in complete accord with subsequent observations, demonstrated the locus from which the ipsilateral responses could be obtained, their association with contralateral movements, and the higher threshold and longer latency for ipsilateral responses as compared with the contralateral.

### (3) *Factors influencing the Ipsilateral Response.*

The various conditions which influence the ipsilateral response may now be considered.

(i) *Anæsthesia.*—It has proved impossible to obtain ipsilateral responses when the animal is anæsthetized with any of the barbituric-acid derivatives (sodium amytal, dial, &c.). This is scarcely surprising in view of the known depressant action of these anæsthetic agents upon the other responses elicitable from the premotor cortex [4]. All successful experiments were conducted under ether anæsthesia, but it was necessary even with ether to ensure light anæsthesia. This circumstance occasionally rendered observation difficult, for if the anæsthesia became so light that spontaneous movements appeared they were prone to confuse the issue. In this connection, however, one extremely interesting observation was made. During the course of an experiment the animal became so light that it began to move both lower extremities rhythmically, as though it were attempting to run. The superior lip of the superior precentral sulcus was stimulated, the ipsilateral lower extremity immediately became fixed in extension, the contralateral in flexion, and this posture was held as long as stimulation continued; as soon as stimulation ceased the running movements began again. The observation was repeated several times with the same result.

(ii) *Ipsilateral response independent of contralateral spinal innervation.*—Because of the consistent association of the ipsilateral response with movements in the contralateral lower extremity the question immediately arose as to whether the ipsilateral response was due to a direct pathway of innervation from Area 6 to the musculature of the extremities of the same side, or whether possibly the ipsilateral response was in the nature of a crossed extensor response secondary to movement (flexion) of the contralateral lower extremity, and thus subserved entirely by a nervous pathway within the spinal cord. This question was particularly pertinent as the ipsilateral response invariably had a longer period of latency than the contralateral and thus always succeeded the latter. That the ipsilateral response may be entirely independent of the contralateral is well demonstrated by the following experiment (one of three, all of which gave the same result).

*Experiment* 2 (*Area* 6 *series, No.* 24).—*March* 20: *Mid-thoracic laminectomy*; *right lateral semisection of spinal cord. March* 21: *Exposure of both hemispheres*; *stimulation right Area* 6, *complex movement left lower extremity, no movement right lower extremity*; *stimulation left Area* 6, *movement left lower extremity, no response in right.*

The subject of this experiment was a small monkey (*M. mulatta*) weighing 1,800 grm.

*Semisection of cord.*—On March 20, 1933, a laminectomy was performed in the mid-dorsal region and a right lateral semisection of the spinal cord was carried out with a small iridectomy knife. The following morning the animal seemed quite normal except for a flaccid paralysis of the right lower extremity. The flaccidity was not complete as there was a slight tendency toward a flexor posture. Nociceptive stimuli applied to the right foot produced a flexion response in that extremity. The knee-jerk was barely obtainable on the right but seemed to have its normal intensity on the left. There was no general response to painful stimuli, pin-prick, pinching, &c., on the left half of the body below the level of the semisection, whereas such stimuli elicited the usual evidences of perception of pain, within the limits of existing paralysis, when applied to the right side.

*Cortical stimulation.*—Following this examination the animal was again anæsthetized with ether and both cerebral hemispheres were exposed. In the subsequent stimulation (Harvard coil) the responses obtained both for monopolar and bipolar stimulation were identical, except that a slightly greater intensity of current was needed with bipolar electrodes.

Stimulation of the motor cortex of the right cerebral hemisphere elicited the usual discrete sustained responses in the left upper and lower extremities. Stimulation of the right premotor cortex with stimuli of slightly greater intensity than those required to excite Area 4 gave rise to the usual complex movements in the contralateral (left) upper and lower extremities. Stimuli applied to the region about the superior precentral sulcus elicited not only contralateral responses but a variety of movements, flexion, extension, pronation, supination, &c., in the ipsilateral (right) upper extremity, but at no time were any movements observed in the right lower extremity.

Stimulation of the left motor area gave rise to typical responses in the right upper extremity, but to none in the right lower extremity. Excitation of the left Area 6, which as usual had a threshold slightly above that of Area 4, produced complex movements in the right upper extremity but none in the lower. Stimuli applied to the cortex about the superior precentral sulcus elicited movements in the ipsilateral upper and lower extremities which were always associated with complex movements in the contralateral (right) upper extremity, but no response was ever observed in the right lower extremity. Stimulation of the cortex immediately above the superior precentral sulcus of the left hemisphere elicited movement in the ipsilateral upper and lower extremities and the contralateral upper extremity simultaneously, but stimuli applied to the inferior lip of the sulcus elicited response only in the two upper extremities.

Following this experiment the animal was sacrificed and the spinal cord carefully examined. The accompanying sketch indicates the extent of the lateral section (fig. 4).

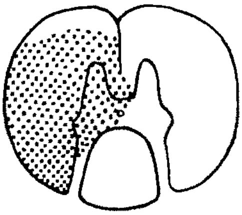

FIG. 4.—Experiment 2. Sketch of a cross-section of the thoracic spinal cord showing the extent of the hemisection of the spinal cord as determined at autopsy.

This and similar experiments definitely established the fact that the ipsilateral response is not dependent upon a local spinal reflex. The response occurs in the absence of any contralateral movement, and conversely the contralateral response could be produced without evoking movement in the ipsilateral extremity.

In addition this experiment showed that the descending pathway essential for the ipsilateral response is limited to the ipsilateral half of the spinal cord. Whether the pathway is doubly decussated in the structures above the spinal cord was not evident from the foregoing experiment. In order to determine this point a further series of experiments were undertaken.

(iii) *Ipsilateral response independent of contralateral cortical innervation.*—In the third operation of Experiment 1 (after Areas 4 and 6 of the left hemisphere had been removed) stimulation of the superior lip of the right precentral sulcus yielded vigorous ipsilateral responses. This and other similar experiments proved that if the impulses responsible for this response crossed to the opposite half of the encephalon only to recross before reaching the spinal cord, the major motor projection systems (Areas 4 and 6) of the opposite hemisphere were not concerned in the response.

Other possibilities, distant as they seemed, had to be excluded, and with that in mind two experiments, of which the following is one, were performed.

*Experiment* 3 (*Corpus callosum series, No.* 9).—*May* 19, 1933: *exposure left cerebral hemisphere*; *elicitation of ipsilateral response*; *section of corpus callosum.*

*May* 22: *Exposure right cerebral cortex*; *elicitation of ipsilateral response*; *extirpation of premotor and frontal areas.*

*May* 31: *Exposure left cerebral hemisphere*; *elicitation of ipsilateral responses. Autopsy.*

The subject of this experiment was a medium-sized monkey (*M. mulatta*) weighing 2,800 grm.

*First operation.—Section of corpus callosum.*—On May 19, 1933, a bone-flap was reflected in the usual manner, exposing the convexity of the left cerebral hemisphere. Stimulation of the motor and premotor areas elicited the usual responses in the contralateral extremities. From a small area on the superior lip of the precentral sulcus stimulation evoked internal rotation of the ipsilateral (left) lower extremity and slight flexion of the digits. The response was limited to this small area and could be repeatedly obtained. The veins draining the left hemisphere into the superior longitudinal sinus were then coagulated and the left hemisphere retracted laterally, exposing the entire length of the corpus callosum. The anterior cerebral artery was occluded with a silver clip and the corpus callosum was sectioned throughout its entire length from the splenium to the genu and including the rostrum. The section was performed slightly to the left of the midline, opening into the left lateral ventricle, in order to avoid any damage to the structures of the right hemisphere. Following this procedure the animal made a rapid recovery and exhibited no marked motor deficit. (See Kennard and Watts [19].)

*Second operation.*—Three days later, on May 22, the animal was again anæsthetized and the right cerebral hemisphere exposed. Stimulation of the motor and premotor areas with a monopolar electrode elicited typical contralateral responses. Stimulation of the cortex about the superior precentral sulcus, which was represented only by a shallow dimple, elicited definite movement in the ipsilateral lower extremity. These movements were comparable to those seen previously from stimulating the left hemisphere. They were somewhat more extensive and consisted of internal rotation of the entire extremity and flexion at all joints. Having made these observations all of the frontal lobe anterior to the motor cortex (i.e., the premotor and frontal areas) was extirpated.

*Third operation.*—On May 31, the animal was again anæsthetized with ether and the *left* hemisphere exposed by reflecting the previously made bone-flap. Stimulation of the superior lip of the precentral sulcus (faradic current from a Harvard inductorium with a bipolar electrode) evoked strong extension at all joints in the ipsilateral lower extremity and feeble flexion of the ipsilateral upper extremity. These ipsilateral responses were associated with strong flexion of the contralateral lower extremity and variable movements in the contralateral upper extremity. The responses were repeatedly obtained from this area but could not be elicited from other portions of the exposed cortex.

The animal was sacrificed and examination of the brain revealed that the corpus callosum had been completely divided.

This experiment confirmed the findings of Experiment 1, and it would seem to exclude quite definitely the possibility that the contralateral hemisphere is essential to the ipsilateral response. The possibility of a double decussation of the pathway in the basal ganglia or brain-stem still remains, but as yet we have been unable to investigate this point.

### (4) *Effect on the Ipsilateral Response of separating Area 4 from Area 6.*

Superficial incision of the cortex separating Areas 4 from 6, and extirpation of Area 4, either abolished or diminished the excitability of the premotor cortex for contralateral responses. It was therefore decided to study the ipsilateral response under such circumstances. Because of the necessity of maintaining very light anæsthesia it was difficult to keep it at a constant level. As slight variations in depth of anæsthesia greatly effected the response the great majority of experiments had to be excluded. However, several which were satisfactory were obtained and the following may be cited.

*Experiment* 4 (*Premotor series, No.* 13).—*Exposure of left cerebral hemisphere; elicitation of usual responses from motor and premotor areas, and movement in ipsilateral lower extremity from superior lip of superior precentral sulcus; superficial incision of cortex separating Areas* 4 *and* 6; *marked depression of contralateral response with enhancement of ipsilateral response; extirpation of Area* 4; *ipsilateral response still vigorous.*

The subject of this experiment was a well-developed, vigorous, though immature, male baboon (*Papio papio*), weighing 4,300 grm.

*Operation.*—On February 24, 1933, the left cerebral cortex was exposed under ether anæsthesia. The cortex was stimulated with a faradic current using a monopolar electrode. As usual the responses from the motor cortex were sustained and discretely localized (threshold 12 cm.). With the coil at 10 cm. typical complex movements in the contralateral extremities could be elicited from the premotor cortex. With stimuli of slightly greater intensity

(9·5 cm.) and light anæsthesia, responses in the ipsilateral lower extremity and tail could be elicited from a small area 1 to 2 mm. in diameter in the posterior part of Area 6 and a short distance above the superior precentral sulcus. The movements of the tail (lateral) were rhythmic. The ipsilateral responses, which were obtained repeatedly, consisted of a sustained extension of the hip and knee and plantar flexion of the foot. These responses were always associated with movement of the contralateral lower extremity, usually extensor in type.

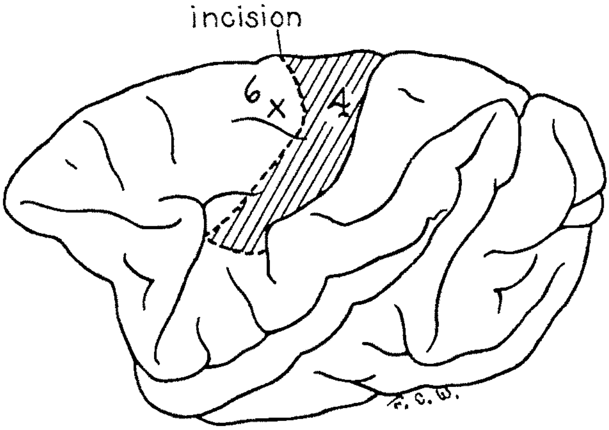

FIG. 5.—Experiment 4. Left cerebral hemisphere of a small baboon, *Papio papio*. "4" indicates Area 4, "6" Area 6 of Brodmann. "X" is the spot from which ipsilateral responses were elicited. The broken line is the site of the superficial incision separating the motor from the premotor area and the cross-hatched area is the motor cortex which was extirpated.

*Incision.*—A superficial incision about 1·5 mm. deep was then made with a sharp scalpel along the boundary between Areas 4 and 6 (fig. 5). Following this incision the excitability of Area 6 for contralateral movements was greatly reduced, but in striking contrast stimulation elicited greatly increased movement in the ipsilateral lower extremity and tail. At times it was possible to elicit movements in the ipsilateral lower extremity without evoking any in the contralateral. This was regarded as especially significant since prior to the incision contralateral movements were vigorous and the ipsilateral were relatively feeble.

*Extirpation.*—Using a sharp scalpel the arm and leg areas of the motor cortex, including the portion on the medial face of the hemisphere, were completely removed (as confirmed by microscopical examination). Immediately following this the excitability of Area 6 was completely suppressed for a short time. The excitability then improved, movements of the ipsilateral extremity and tail continuing with the vigour they had shown following the incision, while those in the contralateral extremity, although still present were limited in extent and elicited with greater difficulty.

The animal made a prompt recovery from the procedure with the usual neurological symptoms from such an ablation.

This experiment was in harmony with our previous experiments which had indicated that the ipsilateral movements were independent of the contralateral, and it also showed that separation of Area 6 from Area 4 increased excitability of the ipsilateral area. As this was in accord with experiments which were being carried out by Dusser de Barenne and Marshall [7], it was decided to adopt their technique in order to obtain a more rigorous control of the results. The animals were anæsthetized lightly with ether and the depth of narcotization kept as constant as possible. Stimuli of constant intensity and duration were then applied once every minute to the point from which ipsilateral responses could be obtained.[1]

*Experiment* 5 (*Area* 6 *series, No.* 16). *Exposure of right cerebral cortex; elicitation of contralateral and ipsilateral responses from superior lip of precentral sulcus; ipsilateral response became weaker and disappeared; novocain applied to motor cortex which soon became inexcitable; return of ipsilateral response with marked vigour.*

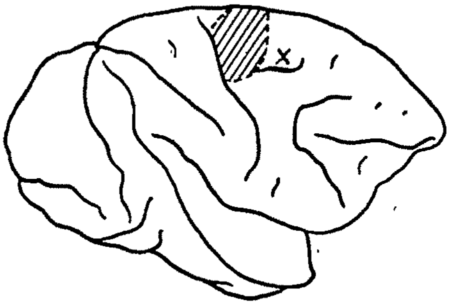

FIG. 6.—Experiment 5. Right cerebral hemisphere, *Macaca mulatta.* "X" is the point from which ipsilateral responses were elicited. The cross-hatched area is the "leg" area of the motor cortex to which novocain was applied.

Under ether anæsthesia the right cerebral hemisphere of a small monkey (*M. mulatta*) was exposed. The ipsilateral response was readily elicited from the superior lip of the superior precentral sulcus. The threshold was determined and the strength of stimulus kept constantly at that level. A series of faradic stimuli of 2·3 seconds duration was applied regularly every minute to the point on the surface of Area 6 (fig. 6) which had given the best ipsilateral response (monopolar electrode).

Initially stimulation of this point gave rise to strong complex movements of the contralateral extremities, usually flexor in type, and definite though not vigorous extensor movements in the ipsilateral lower extremity. During the next ten minutes the ipsilateral response gradually grew feebler until finally it was unobtainable with stimuli of this intensity and duration. A paste-like mixture of 1 per cent. novocain with crystalline toluidine blue was applied to the leg area of the motor cortex (fig. 6). There was no immediate change. But five minutes after the application of novocain the leg area was no longer excitable and a minute later stimulation of the superior lip of the superior precentral sulcus elicited strong ipsilateral responses as well as complex contralateral movement. The ipsilateral responses continued vigorously for about twenty minutes, at which time the leg area of the motor cortex became slightly responsive. The excitability of the novocainized area slowly returned and parallel with it there was a gradual subsidence of the ipsilateral response to its initial level.

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[1] These experiments were carried out in the Laboratory of Neurophysiology under the supervision of Dr. J. G. Dusser de Barenne, to whom we are greatly indebted for having placed his facilities and time at our disposal.

This carefully controlled experiment was confirmatory of the preceding which had been performed with the ordinary technique. It is obvious from these that isolation of that portion of the premotor cortex responsible for the ipsilateral response from the motor cortex lying posterior to it greatly enhances its excitability, but the basis of this effect is not clear from these studies, apart from the fact that it is apparently a release phenomenon. It is to be hoped that Dusser de Barenne and Marshall's more detailed experiments upon a closely related problem will clarify this point.

## II.—ABLATION EXPERIMENTS.

The experiments just described clearly demonstrate that appropriate electrical stimulation of the cortex may give rise to responses of the ipsilateral extremities. The following experiments in which ablations were carried out show that the motor and premotor areas are both concerned in the integration of ipsilateral motor activity.

### (1) *Removal of all but one Motor or Premotor Area.*

Extirpation of the motor area from one hemisphere and of the premotor areas from both, leaving only one motor area intact, interferes with the motor activity, but does not abolish it completely on either side. This is well illustrated by the following experiment:—

*Experiment* 6.—*January* 11, 1933: *Extirpation of left motor area; followed by right hemiplegia which rapidly improved.*

*February* 6.—*Extirpation of left premotor area; increase in right-sided weakness which again recovered.*

*March* 10.—*Extirpation of right premotor area: immediate severe paralysis in all four extremities which slowly improved.*

For this experiment the animal (*M. mulatta*) described in Experiment 1 of of this paper has been selected so that one may correlate more adequately the observations on stimulation with those of ablation.

*Extirpation of left motor area.*—On January 11, 1933, the cortex was exposed under anæsthesia, and after stimulating the ipsilateral area (*see* Experiment 1) the entire motor area and posterior part of the premotor area were removed (fig. 7). Microscopical examination of the extirpated block confirmed the extent of the lesion. Immediately following the operation the right-sided hemiplegia was practically complete. No movement was present in the upper extremity and only very slight movement was seen at hip and knee. The following day the right extremities were much stronger, slight movement having returned to the right shoulder and elbow, and the lower extremity was sufficiently strong to assist in bearing the animal's weight in walking. Within eleven days after the operation the animal was climbing the walls of the cage without great difficulty. The upper extremity continued to be much weaker and less useful than the lower. After four weeks (February 6) the right extremities were used freely for climbing and walking, but digital movements were still impaired.

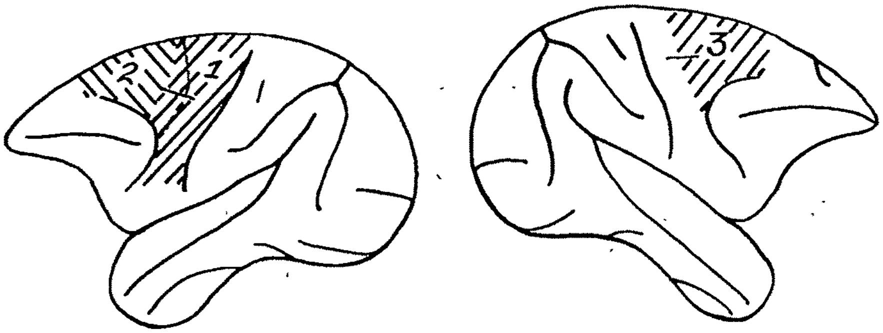

FIG. 7.—Experiment 6. Left and right cerebral hemispheres, *Macaca mulatta.* "1" is the area extirpated at the first operation. It includes Area 4 and part of Area 6. The boundary between these two areas, as determined by microscopical study, is indicated by the broken line. "2" is the area removed at the second operation and "3" at the third. Thus only the right motor area remained intact. All extirpations extended down to the first sulcus on the medial surface of the hemispheres.

*Extirpation of left premotor area.*—On February 6 the left hemisphere was re-exposed and the remainder of the premotor area was removed. Microscopical study of the block extirpated showed that it involved all of Area 6 that remained after the first operation and extended 1 to 2 mm. into the frontal area lying anterior. Though there were no Betz cells in the block removed on February 6 this ablation definitely increased the weakness in the right extremities, but it did not cause them to lapse into the state of profound paralysis present immediately after the first operation. A few hours after the operation the animal was using both right extremities in walking. Five days later the animal ran about the cage and climbed the walls quickly, using all four extremities, although there was obvious residual weakness on the right side. The right extremities were never again used in picking up objects or food. At the end of a month (March 10) one had to observe the animal closely to detect his right-sided weakness (chiefly in the fingers).

*Extirpation of right premotor area.*—On March 10 the right hemisphere was exposed and the entire right premotor area ablated, thus leaving the animal with the right motor area as the only intact portion of its cortical motor projection system. Microscopic examination of the right premotor area indicated that the lesion had extended 1 to 2 mm. anterior to Area 6 into the frontal area. Posteriorly it extended into the anterior part of Area 4 in the upper part.

The immediate motor deficit was quite severe, the animal being able to walk but its movements were very awkward and slow, and both right and left extremities frequently gave way. Marked forced grasping was present in all extremities. Two days after the last operation the animal climbed the wall of the cage, but had great difficulty in descending and finally fell. As the animal attempted to walk it frequently lifted both feet from the floor simultaneously, causing it to fall forward on its face. This poor synchronization of movements in the lower extremities persisted for several months, but the motor deficit slowly lessened. Six days after the operation we first saw the animal grasp food in its left hand and carry it to its mouth. Previously it had eaten by bringing its mouth to the food.

Two months after the third operation (May 15), the animal was very active Its movements were quick though not always well co-ordinated or accurate. It ran about the floor of the cage and climbed the walls with ease: descent, however, was still awkwardly done. After three months, although a definite deficit in motor activity was obvious on close inspection, a casual observer might easily have mistaken the animal for a normal monkey.

This experiment, when considered in connection with Experiment 8, suggests that Area 4 is in fact capable of integrating movements in all four extremities. Similar observations which also support this inference have been reported in another connection by Fulton and Kennard [12]. The next experiment shows that Area 6 may function vicariously in the same way although not as effectively.

*Experiment* 7[1] (*Premotor series, No.* 10)—*November* 7, 1932: *Exposure left cerebral hemisphere*; *extirpation of motor area*; *marked right hemiparesis with partial recovery.*

*November* 21: *Exposure right cerebral hemisphere*; *extirpation motor cortex; marked weakness in left extremities which gradually improved.*

*December* 5: *Extirpation left premotor area*; *increase in motor deficit on right side and appearance of forced grasping.*

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[1] We are much indebted to Dr. M. A. Kennard for her permission to incorporate this experiment in this report.

The subject of this experiment was a small female baboon (*P. papio*) not yet mature, weighing 3,900 grm.

*Extirpation of left motor area.*—On November 7, 1932, the left hemisphere was exposed under amytal anæsthesia, and after stimulating the exposed cortex the motor area (see fig. 8) was removed. The following day there was a complete flaccid paralysis of the right upper extremity, and although the lower extremity was very weak it was sufficiently strong to aid in fairly rapid progression. Movement in the right lower extremity was limited at first to the hip and knee, but gradually the limb increased in strength and power returned at the ankle and foot. Not until four days after operation was any movement observed in the upper extremity, and even then it was slight and limited to the shoulder and elbow. By the twelfth day movement in the right lower extremity was sufficient in strength to serve adequately in running and standing. The upper extremity, however, was never used in progression, and almost no movement was observable at the wrist or in the digits.

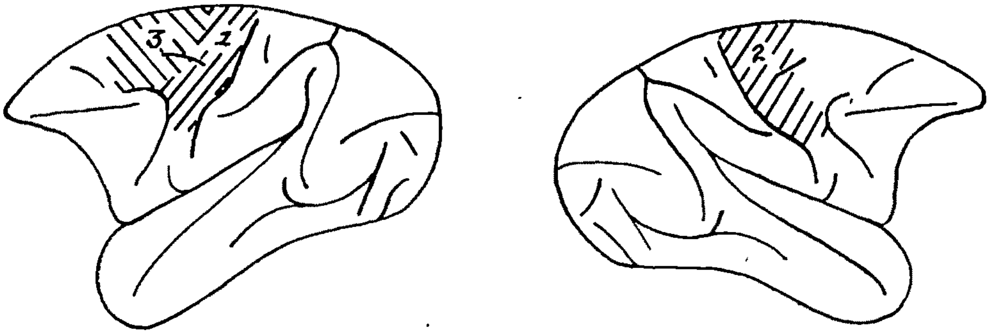

FIG. 8.—Experiment 7. Hemispheres of small female baboon, *Papio papio* "1," "2" and "3" denote the areas extirpated at the first, second and third operations respectively; only the right premotor area was left intact.

*Extirpation of right motor area.*—On November 21 the right hemisphere was exposed under amytal anæsthesia, and after the usual exploratory stimulation of the cortex a block including the entire motor area, and encroaching somewhat upon the premotor, was extirpated (fig. 8, right-hand diagram). The following morning the animal was sitting up in the cage, and when released it immediately progressed across the floor of the room and climbed the wall of another cage. Its favourite method of progression at this stage was to lie on its abdomen on the floor and push itself along with sweeping movements of the extremities which resembled swimming. The deficit was not much greater in the left extremities than the right, and movement was present in all four. It made no effort to bring food to its mouth with its hands, but other evidences of recovery of the use of its extremities were plentiful; within a few days it was able to stand. However, in running the two upper extremities or two lower extremities moved simultaneously, resulting in a peculiar hopping gait.

*Extirpation of the left premotor area.*—On December 5 the left hemisphere was again exposed under amytal anæsthesia and the entire left premotor area was extirpated, leaving the right premotor area as the only remaining portion of the cortical motor projection systems. The following day the animal was able to sit up and to run about the room in a fashion much similar to that prior to the last extirpation. However, its movements were slower and its extremities weaker. Reflex grasping appeared for the first time, but rigidity was not evident until two days later and involved the right extremities primarily. This unilateral extensor rigidity on the right caused a tilting of the body to the left as the animal walked or ran. The left upper extremity was now frequently used by the animal to feed itself, whereas the right was never used to pick up objects.

In the preceding two experiments animals were observed with either one motor area or with one premotor area remaining intact. Although their motor activity was far from normal they were not completely paralysed in any of their four extremities, since they were able to perform, rather crudely to be sure, most of the gross movements of normal animals.

### (2) *Bilateral Removal of Motor and Premotor Areas.*

In striking contrast with these are the animals from which the motor and premotor areas have been completely removed on both sides. Such a preparation is completely paralysed, i.e., it cannot sit, stand or run, and it is quite unable to feed itself. Indeed its motor activity is reduced to that of a thalamic preparation (Bieber and Fulton [1]) consisting of stereotyped grasping and groping movements which have been interpreted as exaggerated righting reflexes.

*Experiment* 8 (*Area* 6 *Series No.* 1).—*January* 5, 1933: *Exposure of left cerebral hemisphere; extirpation of motor area; marked right hemiplegia which gradually improved.*

*January* 26: *Extirpation left premotor cortex; increased weakness in right extremities which again improved.*

*February* 9: *Exposure right cerebral hemisphere; extirpation entire motor and premotor areas; complete quadriplegia: death seven days later.*

*Extirpation of left motor area.*—On January 5, 1933, the animal, a mature female monkey (*M. mulatta*) weighing 4,100 grm., was anæsthetized with ether and the left cerebral hemisphere exposed. After exploring the excitability of the cortex, the entire motor area, including the face representation and a small portion of the premotor area, were extirpated (fig. 9). The extent of the ablation was determined by microscopical examination of the block. On the evening of the day of operation the right upper extremity exhibited a profound flaccid paralysis; there was slight movement, however, at hip and knee. The following morning slight movement was present at the shoulder and elbow, and both extremities could be used to bear the animal's weight in progression. Subsequently the right extremities continued to improve in strength and usefulness, though not so rapidly as during the first twenty-four hours. Three weeks later, though employed in walking, running and climbing, the extremities were never used in grasping food or bringing food to the mouth, and all movements on the right were slower and more awkward than on the left side.

*Extirpation of left premotor area.*—On January 26 the left hemisphere was re-exposed, and the left premotor area, which proved to be electrically excitable, was extirpated (fig. 9). Microscopical study of the block indicated that the extirpation was restricted to Area 6. On the evening of the operation the animal was able to stand upright and climb the walls of the cage, using all four extremities. There was, however, considerable increase in motor weakness of the right side, and a reflex grasping appeared for the first time in the right upper extremity. Motor power of the right side improved considerably during the first few days and then remained stationary. Two weeks after this operation, although the animal was in excellent condition and climbed rapidly about the walls of its cage, it used the right extremities relatively little, the lower being utilized to much better advantage than the upper, which served more as a prop than for prehension.

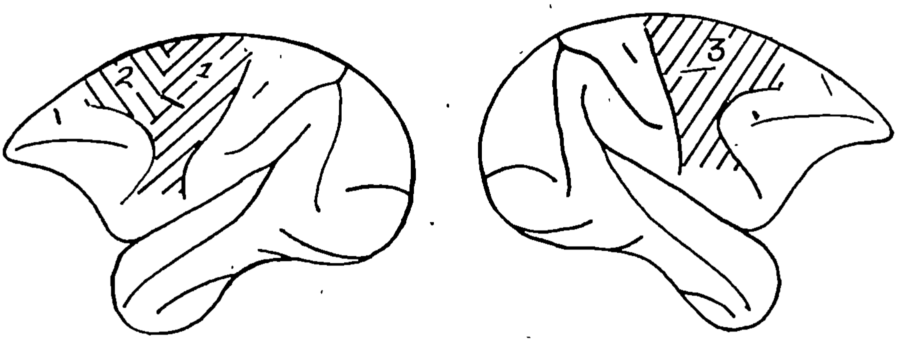

FIG. 9.—Hemispheres of mature female monkey, *Macaco mulatta.* "1," "2" and "3" denote the areas removed at the first, second and third operations respectively. The motor and premotor areas, which contain the major motor projection systems of the cortex, were thus removed bilaterally.

*Extirpation of right motor and premotor areas.*—On February 9, the right hemisphere was exposed, and after identifying the excitable areas by faradic stimulation the entire motor (including *face*) and premotor areas were extirpated in a single block. The extirpation involved not only the area on the convexity of the hemisphere, but extended down to the first sulcus (*sulcus cinguli*) on the medial surface.

Following this procedure, volitional power in all four extremities was completely abolished, and the neurological status was thus in striking contrast to the condition shown in Experiments 6 and 7. The animal lay quietly on whichever side it was placed. At the approach of an observer it might bare its teeth or turn its head slightly, but it made no movement with its extremities. As its facial and masticatory muscles were paralysed, it could not take food even when presented to its mouth, and food placed in its mouth remained there, rendering a stomach tube necessary for feeding. There was at first no movement in the extremities. Later, however, paroxysmal rhythmic groping movements appeared in the upper extremities. If during these movements the hand came in contact with an object, it immediately grasped it, the groping stopped and the grasp continued indefinitely, often for hours. As the animal lay upon its side, its postural pattern remained always the same. For example, if it lay upon the left side, the left upper and lower extremities would be rigidly extended, the right markedly flexed. If it was turned over on to the right side, the pattern would become reversed. Although these reflex alterations in posture (fully described by Bieber and Fulton [1]) were always present, practically no other movement except the paroxysmal groping was ever observed. The animal was unable to sit, stand, walk, climb, eat or to perform any of the activity seen in normal monkeys, or even in those described above in which only one motor or premotor area remained.

This picture remained unchanged, and on February 16, one week after the operation, the animal was found dead in its cage, lying on its left side with the postural pattern described above and strikingly accentuated by its rigor mortis. At necropsy an intussusception was found at the lower portion of the ileum with evidence of intestinal obstruction—the commonest cause of death in animals having bilateral lesions of the premotor area (Watts and Fulton [24]). The brain, which was in good condition, was carefully studied grossly and microscopically, and the lesions were found restricted to the region of the cortex originally ablated at operation, i.e., there was no softening of surrounding areas or of the deeper nuclei.

Five other animals have been similarly prepared in the laboratory. In some, considerable activity in mastication and swallowing has been preserved by leaving a portion of the face area intact (thus minimizing nursing care), but all have presented a similar completely incapacitating paralysis of the extremities from which they never recovered, although two of them survived for as long as four months (Bieber and Fulton [1]).

The ablation experiments are thus in harmony with the stimulation experiments. Together they demonstrate that one motor area, or one premotor area, is alone capable within certain limits of integrating movement in all four extremities, i.e., ipsilateral as well as contralateral. When the one remaining area is removed the animal becomes helpless and devoid of all motor activity of a volitional character. Whether all of one motor cortex or premotor cortex, as the case may be, is necessary for the maintenance of motor activity in the extremities is undetermined. In view of the stimulation experiments it is possible that animals in which only that portion of the cortex about the superior precentral sulcus remained intact would be capable of volitional activity in the ipsilateral extremities.

## III.—DISCUSSION.

### (1) *Correlation with Previous Studies.*

During the twenty years immediately following the demonstration by Fritsch and Hitzig in 1870 and by Ferrier in 1873 that motor manifestations could be elicited by electrical stimulation of the cerebral cortex, numerous investigators studied the excitability of the cortex. Many observers elicited and recorded responses in the extremities ipsilateral to the area stimulated. The results of these experiments are adequately summarized by Gotch and Horsley [15] and it was their opinion that there was no representation of the ipsilateral extremities in the cortex but that movements elicited on the same side were due to bringing "other portions of the central nervous system, particularly the opposite excitable cortex, the cerebellum and basal structures" into play. How this influence upon other centres was achieved, whether by transmission of nervous impulses or spread of electrical effect, they did not state. However, it is difficult to interpret these early observations since the strength of current used for stimulation was far in excess of that in the carefully controlled experiments of modern workers. This is well illustrated by the work of Gotch and Horsley just referred to. In their experiments the typical response to stimulation of the motor area is referred to as "tonic followed by clonic contractions" [15, p. 350]. This is an effect commonly observed in response to strong stimuli and frequently referred to nowadays as "epileptiform after-discharge." That Gotch and Horsley were referring to a similar response is evidenced by their reference to the results of stimulation as "slight fit," "good fit," &c. [p. 351]. It is also of interest that many other workers [*e.g.* 25] elicited ipsilateral responses in dogs, rabbits and rodents as well as monkeys; and that these responses were obtained after section of the corpus callosum and other commissures, after removal of the opposite hemisphere, and after a variety of lesions of the spinal cord.

In 1899 Hering elicited ipsilateral movements from the cerebral cortex of both dogs and monkeys ("*M. rhesus* and cynocephalus baboons"). In dogs ipsilateral responses could still be elicited after section of both pyramids and hemisection of the medulla. In monkeys ipsilateral movements were evoked by stimulation of the cortex after section of both pyramids. It is of considerable interest that in Hering's experiments the region about the superior precentral sulcus (which he called sulcus X) was the area from which these responses were obtained. In 1902 Rothmann [21] confirmed these findings but added little new information so far as the ipsilateral response is concerned.

During the last twenty years there is almost no reference to the excitability of the cerebral cortex for ipsilateral movement.

In 1919 C. and O. Vogt [23] stated very briefly that they had elicited ipsilateral responses by stimulation of the premotor cortex. "Die Bewegung neigt mehr als bei Reizung des Hauptfeldes (Area 4) dazu, sich auch auf die gleichseitige Extremität zu erstrecken. Ja, man beobachtet gar nicht selten sogar die Reaktion zunächst in der gleichseitigen Korperhälfte." We are not aware of any more detailed reference to this point by these authors.

However, other evidences of control over the ipsilateral extremities by the motor projection systems have from time to time appeared. In 1917 Leyton and Sherrington [20] demonstrated that a lesion of the excitable area of the cortex results not only in degeneration in the fibres of the lateral pyramidal tract of the opposite half of the spinal cord, but to a lesser extent in the lateral pyramidal tract of the same side as well. They were, however, unable to associate this with their experiments of stimulating the motor area or with the paresis which follows removal of the motor area. Their failure to obtain ipsilateral response upon stimulating the motor projection area is possibly explainable on the basis of deep anæsthesia. In the experiments reported here it has been repeatedly demonstrated that any but the lightest ether anæsthesia will destroy the response, certainly narcotization sufficient to suppress the excitability of Area 6 would do so.

Recently Fulton and Keller [11] have confirmed the findings of Leyton and Sherrington [20] in various primates. They have summarized their findings as follows [11, pp. 128-129] :—

" In the cat and dog there is no evidence to suggest that removal of the motor area, or even of a whole hemisphere, influences the motor power of the ipsilateral extremity; bilateral lesions tend, in fact, to be less disturbing to locomotion as a whole than are unilateral lesions. In the monkey destruction of the second leg area appears to have little influence upon the power of the ipsilateral extremity, but the baboon suffers definite and permanent impairment in ipsilateral motor power when this operation is carried out. This is also true of the gibbon. The resting posture of the extremities is also changed (abnormal adduction of the thighs, extension and lateral deviation of the toes).

"In the chimpanzee, destruction of the second leg area yields a marked deficit in ipsilateral motor power, and a profound and permanent alteration of posture of the lower extremities. Our data on the comparative rate of recovery of motor power in the various primates following ablation of the second leg are as yet incomplete, but it is clear: (1) that the second extremity requires nearly three times as long as the first to regain flexor power at hip and knee; and (2) that the chimpanzee is at least twice as slow to regain a corresponding degree of power as the baboon. We therefore conclude that the baboon, gibbon, and chimpanzee have some degree of bilateral representation in the leg area."

Attention was also drawn to the report of human cases by Holmes and Sargent[17], from which it was concluded that "It is evident . . . that paralysis following bilateral injuries to the foot area was more extensive and less quickly recovered from than one would expect on the basis of recovery of motor power which generally follows injury to a single leg area." Additional evidence in human cases has recently been presented by Gardner [14]. Following the removal, because of an infiltrating glioma, of a large part of the right hemisphere, exclusive of the major part of the basal ganglia, the patient immediately suffered a complete left hemiplegia. However, in about three weeks evidence of voluntary movement appeared in the left lower extremity. This progressively increased until within a comparatively short time the patient was able to walk with the aid of a cane. Recently Dr. M. M. Peet, of Ann Arbor, Michigan, has informed us of a case of his from which the entire hemisphere was removed including the basal ganglia, and within twenty-four hours unmistakable evidence of voluntary movement was present in the contralateral extremities. It is to be hoped that he will see fit to report this case in greater detail.

Dandy [6], in reporting five cases from which he removed a large part of the right cerebral hemisphere, states that Case 1 which survived the operation two years and two months showed "slight flexion and extension of the knee and thigh. . . . but there was never enough function to be of service." Unfortunately no details are supplied concerning the extent of the extirpation.

Obviously it cannot be concluded from the report of these three cases that the movement which appeared in the extremities contralateral to the extirpation was due to innervation by the intact ipsilateral hemisphere. However, the experimental findings here reported would clearly support such a hypothesis.

Of even greater interest in connection with human material is the isolated statement made by Otfrid Foerster [8] in his London lectures of 1931 that the thigh is often represented bilaterally in the cerebral cortex. This he determined by electrical stimulation of the cerebral cortex of over one hundred and fifty human subjects.

In summary then, it is clear from a review of the literature that many workers have elicited ipsilateral responses from the cerebral cortex of a wide variety of animals and under many different circumstances. Clinical observations suggest that in man the cerebral hemispheres are capable of ipsilateral innervation, but it may not be as extensive as in monkeys. In no human case where a large part of one hemisphere has been removed has the motor activity which developed subsequently in the paralysed member been comparable in degree to that seen in infrahuman primates. Yet essentially the recovery is of the same nature. The pathway of ipsilateral innervation in man is unknown, but it is not unlikely that it is identical with that present in the sub-human primates.

### (2) *Interpretation of Experimental Data presented in this Paper.*

These experiments demonstrate that in the monkey electrical stimulation of the premotor cortex in the region of the superior precentral sulcus evokes movement in the ipsilateral extremities, particularly the lower, which in the intact animal is associated with complex movements of the contralateral extremities. That the ipsilateral response is independent of the contralateral extremities has been demonstrated by appropriate hemisection of the spinal cord which abolishes the contralateral response while leaving the ipsilateral unchanged (Experiment 2). The pathway concerned in these reponses is independent of the pyramidal tract from the same hemisphere as shown by cases in which it has been produced after Area 4 has been removed (Experiment 4). The pathway does not pass through the corpus callosum and is independent of Areas 4 and 6 in the opposite hemisphere (Experiments 1 and 3). Its course through the brain-stem is undetermined, but if it does cross to the contralateral half of the neural axis the decussation must be a double one, for the pathway occupies the ipsilateral half of the spinal cord (Experiment 2).

Isolation of the portion of the premotor cortex responsible for the ipsilateral response from Area 4 by incision of the cortex, extirpation of or application of novocain to the motor cortex, has in several instances greatly enhanced the ipsilateral response (Experiments 4 and 5).

Ablation experiments, moreover, are entirely in harmony with the results of stimulation. The motor or premotor area of one hemisphere is sufficient to integrate movement in all four extremities (Experiments 6 and 7), but on the removal of Areas 4 and 6 from both hemispheres the animal becomes helpless (Experiment 8), all volitional power being destroyed.

## IV.—CONCLUSIONS.

(1) Ipsilateral responses in the extremities can be readily elicited in monkeys by stimulation of the cortex in a restricted region about the superior precentral sulcus. The excitable area lies principally in Area 6 of Brodmann, but it may extend into the anterior limit of Area 4.

(2) These ipsilateral responses are independent of the contralateral responses with which they are often associated and are mediated by a pathway which is entirely ipsilateral (unless there be double decussation within the brain-stem).

(3) Either Area 4 or Area 6 alone in one hemisphere is capable of cortical integration of movement in all four extremities; an animal with Areas 4 and 6 removed from both hemispheres is totally incapacitated.

(4) There is evidence of ipsilateral innervation of the extremities in man which is probably mediated by a pathway comparable to that demonstrable in monkeys.

*Addendum.*—After this paper had gone to press, Professor Sherrington kindly drew our attention to the remarkable early paper of Wertheimer and Lepage [25] who observed ipsilateral responses from the motor cortex of dogs after contralateral semisection of the spinal cord.

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## NOTICES OF RECENT PUBLICATIONS.

*Traité de Physiologie Normale et Pathologique. Système Nerveux* (Première Partie). Paris: Masson et Cie. 1933. P. 566. Price 100 fr.

The ninth volume of Roger and Binet's System of Physiology is devoted to the nervous system, and in the tenth, the early appearance of which is promised, it will be completed.

This volume differs in scope and aim from the textbooks or treatises on physiology with which English readers are familiar, for in addition to dealing with the normal functions of organs as determined mainly by experiments on animals, it describes, frequently in considerable detail, the effects of disturbances of these functions, particularly as seen in man. In one of the early chapters on the degeneration and regeneration of peripheral nerves, for instance, the methods of surgical suture of injured nerves in man is discussed at length, and the next chapter on the disintegration of nervous tissues is wholly pathological. This combination of the physiology and pathology of organs in the one volume is, however, particularly useful to the clinician, for it enables him to turn at once from the normal to the abnormal and therefore to obtain a wider and more circumspect view of the questions interesting him than he can find in textbooks of clinical medicine or pathology.

Another feature of this volume which should appeal to neurologists is that many of the chapters are written by clinicians who are familiar with the needs and difficulties experienced in practical medicine: Alajouanine, Bertrand, Lévy-Valensi and Lhermitte are among the contributors of special sections.

The first chapters deal with the neurone and the fundamental functions of nervous tissue; the treatment of this subject is admirable: it is concise but adequate for the needs of the physician. The sections on the reflexes and on tropism are written in more detail, the former including an excellent subsection on the conditioned reflexes. The chapters on sensory and motor functions and on cerebral localization do not reach such a high standard and are in many ways disappointing. Only two pages are devoted to the sensory paths in the brain and the nature of the representation of sensation in the cortex in the former, and little more in the latter, and in both the discussion on the many disputable points involved is inadequate. Lhermitte's chapter on the central ganglia is excellent; clear, critical and comprehensive from both the clinical and experimental points of view. The sections on convulsions by Richet, and on sleep by Legendre, are also valuable contributions. The last sixty pages are devoted to the biochemical study of general anæsthesia.

This volume would have been more useful if there had been adequate bibliographical references to all the chapters, but it can be strongly recommended as an introduction to clinical neurology and as a work of reference.

*General Principles of Human Reflexology.* By V. M. BECHTEREV. Translated by E. and W. MURPHY from the 4th Russian Edition. Pp. 467. London: Jarrolds. 1933. Price 21s.

Bechterev is known in England chiefly through the French and German translations of his books on the anatomy and functions of the nervous system, but he was also, and particularly in his late years, interested in psychology and its medical and social applications. The sub-title of this volume, "An Introduction to the Objective Study of Personality," indicates its aim; it contains a presentation of his views based on his studies extending over many years, and especially during the time he was Director of the "State Reflexological Institute" in Leningrad.

By reflexology Bechterev meant the study of human personality from the strictly objective standpoint by the observation of the individual's reactions to external and internal stimuli of the present or of the past. He insists that the interpretation of the observations must be based on neurology, or what we know of the structure and functions of the nervous system, and must be independent of "subjective psychology" to which he denies any value in the investigation of scientific problems. From the correlation of the individual with his environment he later extended his methods to the study of communities, an attempt which he called "collective reflexology."

Bechterev's reflexology is obviously related on the one hand to Behaviourism, but he insists that they are not co-extensive in method or in aim, and on the other to the work of Pavlov's school on the conditioned reflexes. He does not, however, accept many of the data obtained by Pavlov's methods or their interpretations, and often refers disparagingly to them. So-called "association reflexes" are the basis of his theories: they include all correlative processes from the highest to the lowest and are conformable to laws. By these laws all activities of the nervous system are explained. The reader of this volume will, however, feel that many of the author's statements and hypotheses are not satisfactorily supported by experiment or argument. Inhibition, for instance, is a temporary blocking of correlative activity; sleep is a defence or protective reflex inhibitory in character; thought and subjective experiences are inhibited reflexes. The lack of adequate demonstration of such hypotheses is the most disappointing feature of the book. Further, there is no clear or concise indication or description of his methods of "reflexological" investigation in man, and the lines along which he reached his conclusions are therefore often obscure. Other annoying features of the book are the failure of logical sequence in dealing with various subjects, the frequent references, sometimes acutely controversial, to matters scarcely germane to his thesis, and the recurring claims to priority in discovery or investigation.

The book contains much interesting material, but it is doubtful if it adds anything to our knowledge of the activities of the human brain or mind, or if it will contribute to the solution of the many problems dealt with in it. The translation has evidently been carried out with care and is readable.

*Clinical Examination of the Nervous System.* By G. H. MONRAD-KROHN. London: H. K. Lewis. Sixth Edition. Pp 234. 1933. Price 7s. 6d.

The sixth edition of this useful handbook is little altered as compared with its immediate predecessor. Small additions which have become necessary by the advance of knowledge or by further experience may be found in its pages, and a few corrections have been made.

Its chief worth still lies in the fact that it is founded on the author's own practical experience, and it is therefore a safe introduction for the student into clinical neurology.

*Die Kombinierte Enzephal-Arteriographie.* Von W. LÖHR und W. JACOBI. Leipzig: G. Thieme. 1933. S. 82. Price 16 M.

The injections of strong solutions of sodium iodide into the carotid artery, as introduced by Moniz, has in some cases led to unpleasant results and is, according to the authors of this monograph, unreliable. Thorotrast, which they have used, is safer and more effective; they claim it entails no risk, does not produce spasm of the vessels and later reactions do not occur. They have employed it in more than 250 patients and have seen no complications. They advise, however, except in the case of a suspected tumour and raised intracranial pressure, the combination of encephalography with arterial injection, as in the radiographic pictures the distribution of the arteries and the size and shape of the ventricles can be studied simultaneously. The technique of carotid injection and the distribution of the cerebral arteries as visible in arteriograms are fully described, and numerous radiographs are included to show the changes in general paralysis, epilepsy, arteriosclerosis, hydrocephalus and cerebral tumours.

The printing of this monograph and the reproduction of the illustrations deserve high praise.

*La Spirochétose Méningée.* Par J. TROISIER ET Y. BOQUIEN. Paris: Masson et Cie. 1933. Pp. 187. Price 34 frs.

In this monograph an interesting form of benign meningitis is described which is due to infection by the spirochæta ictero-hæmorrhagica of Inada and Ido, the causal agent in fact is that of the recurrent febrile jaundice with which we became acquainted during the war. The onset is sudden and the symptoms those of an acute meningitis. It is chiefly young males who are affected, and most of the cases have been observed in the late summer. The cerebrospinal fluid is generally clear, but may be turbid if there is a large collection of polymorphs. The number of cells in it varies and apparently bears little relation to the severity of the attack. At first polymorphs predominate, but later these may be only lymphocytes. The protein content of the fluid is proportionately lower than that of the cells. All cases recover, but there are frequently recurrences of the symptoms. Occasionally slight jaundice is present, and in a few cases the kidneys are affected. Injection of the cerebrospinal fluid into guinea-pigs may produce the lesions characteristic of spirochætosis ictero-hæmorrhagica, and in all the cases accepted by the author the serological tests were positive.

The relation of this form of meningitis with the benign lymphocytic meningitis, many cases of which have been recently observed in England and elsewhere, is interesting. The authors do not admit the identity of the two conditions, but the symptoms, the clinical course and the changes in the cerebrospinal fluid are remarkably similar in the two conditions.

*De la Psychose Paranoiaque dans ses Rapports avec la Personnalité.* Par JACQUES LACAN. Paris: Le François. 1932. Pp. 381. Price 50 fr.

This rather pretentious monograph is an attempt to give a theoretical interpretation of paranoia and to describe a new clinical type. It would be more valuable if the authors conception of paranoia were more strictly in accordance with the orthodox view; this defect is particularly evident in the case of Aimée, reported and discussed at length, who presented, according to the author, the hitherto undescribed type, "paranoia d'auto-punition." Most psychiatrists would be very willing to concede the curability of her condition, while denying that it conformed to any type of paranoia. The first part of the book discusses the conception of paranoia and contains a critical examination of the various theories. The case of Aimée, and the conclusions which the author arrives at concerning the symptoms, psychopathology and the treatment of the condition follow. An account of the methods of examining the personality of psychotic patients concludes the book, which is wordy and lacking in the usual French lucidity of expression.

*Nouveau Traité de Psychologie.* Par GEORGES DUMAS. Tome deuxième. Paris: Alcan. 1932. Pp. 612. Price 100 fr.

This second volume of a most promising succession deals with the foundations of mental life. To be thorough and, at the same time, critical and concise, is the counsel of perfection which its contributors have for the most part happily followed.

The first book, which is short, deals with the elementary reactions—reflexes, maintenance of tone, muscular activity and secretory responses to psychic stimuli: Dumas, Piéron and André Mayer are responsible for these. The physiology of the special senses is the subject of Book II, by Bourdon; it is competent but, like the preceding book, too brief to be exhaustive. Book III, on affective states, begins with a chapter on the Agreeable and the Disagreeable, and another on Pleasure and Pain, by G. Dumas. These are instructive but partial. The chapters on Emotion and Primary Needs are by the same writer, whose presentation is largely influenced by physiological considerations; it is thus in marked contrast to such an exposition of the same subject as that of Störring in the "Abderhalden Handbuch." Instinct is discussed briefly by Languier des Bancels, without reference to the views of von Monakow and some others of note. Book IV, with which the volume ends, consists of an admirable account of the Psychology of Imagery by Myerson, who shows a remarkable grasp of the relevant literature. It is a great pity that neither of the two volumes issued so far in this series has been provided with an index of subjects or proper names; otherwise the production is excellent.

*The Growth and Variability of Intelligence.* Part I by C. A. Richardson. Part II by C. A. Richardson, and C. W. Stokes. *British Journal of Psychology,* Monograph Supplement. London: Cambridge University Press. 1933. Pp. 83. Price 8s. 6d.

The growth of intelligence in children, as measured by intelligence tests, is not to be judged from an ordinary curve of norms, since the individual test items may have different values. The method which was suggested by Thurstone for overcoming this defect is here examined in detail; the material for the study was obtained by the application of group tests, devised by one of the authors, to some 12,000 children. The evidence pointed towards the correctness of Thurstone's conclusions, that the absolute variability of intelligence increases with age and that the spread of intelligence at any age is proportional to its mean level at that age. The second part of the study, which is mainly mathematical, is an attempt to discover whether the ability growth curves obtained from the results of the various test items correspond to the curve for natural growth processes, as described by Courtis. The authors find in general that intelligence tests are far more delicate instruments than is usually thought.

*Soziale und Persönliche Bedingungen des Chronischen Alkoholismus.* von Kurt Pohlisch. Leipzig: Thieme. 1933. Pp. 52. Price M. 5.20.

The author has for years been occupied with the psychiatric aspects of alcohol, and here points out that the ætiological problem of these psychoses has by no means been solved when the alcoholic factor has been demonstrated. In the first part of the book he discusses the general social influences which bear on the problem of drinking and refers to the social methods of diminishing alcoholism in the general population. He appears to be unacquainted with the large English literature concerned with alcoholism, especially in its social aspects. In the second part, on the personal factors in chronic alcoholism, the physical and mental constitution of the drunkard receive concise but adequate attention, and the genetic evidence is presented, with the familiar references to Agnes Bluhm's work; the uncorrobative English experiments are not mentioned. The book as a whole is a praiseworthy summary of the problem as it presents itself in Germany.

*Studies in Sociology.* By MORRIS GINSBERG. London: Methuen. 1932. Pp. 211. Price 6s.

Sociology, as Professor Ginsberg shows in his opening chapter, covers a wide field not yet well-defined. Its basis must be looked for in biology and sociology, to certain aspects of which the greater part of this book is devoted. After chapters on history and social purpose, the author examines the conception of evolution in sociology and the problems of instinct and emotion; there is also a critical examination of the assumptions on which eugenics is based.

*Science et Morale dans les Problèmes Sociaux.* Par A. MOCHI. Paris: Alcan. 1931. Pp. 583. Price 60 fr.

The aim of this book is to apply the scientific method to the solution of social problems which the author regards as essentially moral problems, and to substitute for current sociology a universally accepted positive scheme of morals based on observation and experiment. The attempt is unsuccessful, but it is a lucid contribution; actually the treatment is semi-philosophical, and the subject matter mainly political.

*On Mental Hygiene.* By JOSEF LUNDAHL. Copenhagen: Levin and Munksgaard. 1932. Pp. 299. Price Dan Cr. 12.

Dr. Lundahl died in 1930, leaving this book unfinished, but those who knew of his work in Gotland thought that the manuscript should be published as he had left it, without revision. Many aspects of mental hygiene are considered here in the light of his work at Visby; the section on "boarding-out" and the case histories are of particular interest.

*Diseases of the Nervous System.* By W. RUSSELL BRAIN. Oxford Medical Publications, Oxford University Press. London. 1933. Pp. 899. Figs. 50. Price 27s. 6d.

The writer of a medical textbook works within narrow limits. He has to keep in mind the particular category of medical readers for whom he is writing, and to be clear as to the service he intends to render them. Having defined his task he must keep himself ruthlessly to it. The crux of the medical writer's problem to-day is not what he is to include, but what he should omit. It is a defect of some modern textbooks that their authors have never formulated their problem in these terms, and have left it obscure as to whom they wish to reach.

There is another point in which the modern textbook writer differs from his predecessors. In the period when Gowers wrote his still unequalled textbook of nervous diseases, the author prepared himself for his task by a long apprenticeship in the practice of medicine. He wrote because he had something to impart, and not simply because there was room on the market for a a book on his subject. His book crystallized his own experience. It was not a compilation. A textbook of the first rank can be written on no other foundation, and the authority of much current medical writing suffers by the departure from this sound principle.

If we take Gowers' book, or that of Murchison on "Continued Fevers," and compare the vivid clinical descriptions they contain with a typical clinical statement in the average modern textbook, we realize that the older writers have given us of the fruit of their observation, the modern writer but a lifeless compilation. The old books have the breath of life still about them, the new one smells only of the lamp.

In the matter of the special textbook for student and practitioner, a new standard has recently been set by Lewis's "Diseases of the Heart." Here the author has ruthlessly stripped his subject of non-essentials. Yet in the matter of diagnosis, prognosis and treatment he provides all the doctor needs to carry with him to his work. He has made the subject as simple as possible, he has set out to help rather than to dazzle the practitioner.

Dr. Russell Brain's book is presumably intended for the same categories of reader, but its plan and scope are not those of Lewis's work. On the contrary, it attempts to embody all the most recent and recondite advances in neurology and neuropathology, the speculative as well as the established. From "ginger paralysis" to "Australian X disease," all the rarest affections of the nervous system—though the practitioner may never hope to encounter them—have their chapters. Nothing has been missed, and the result is rather a concise encyclopædia than a working guide to neurology. Anatomy and physiology, too, have been treated at unusual length, though even the most ardent advocate of such a foundation to clinical neurology would admit that much of both these subjects is of purely academic interest and lacks practical application.

When the practitioner looks up the chapter on paralysis agitans, he wants to know how to identify the malady, how he may expect it to behave, and what he is to do for his patient. He does not want, and will certainly not read, the several difficult pages upon the anatomy and (highly speculative) physiology of the corpus striatum with which the author provides him. Nor is this matter adequate to the needs of the professed neurologist. What purpose, then, does it serve?

In the difficult matter of proportion, also, a sound balance has not been struck. More space is devoted to the technique of alcohol injection for trigeminal neuralgia than to an account of the manifold pictures of cerebral vascular disease, or those of disseminated sclerosis, to name but two items of great practical interest to the practitioner. Few practitioners will, we hope, venture to inject for trigeminal neuralgia, but all need to be familiar with these constantly recurring clinical problems.

Further, in embodying the new in his book, the author has not always omitted the views which this has rendered obsolete. The chapter on poliomyelitis is an example of the confusion arising from an attempt to mix the old and the new.

Nor is the book free from contradictions upon important points. Thus, on p. 248 we read that intracranial gumma does not respond to antisyphilitic treatment and should be dealt with as any other neoplasm. On the following page, the reader is advised to employ intensive antisyphilitic medication for this same lesion.

More important than these criticisms of detail is the doubt we must feel as to the book's purpose. It provides too much and too indiscriminately for the practitioner, too little and too superficially for the neurologist.

The figures are of unequal merit and on the whole are inadequate.

*The Mechanism of Nervous Action.* By E. D. ADRIAN. Oxford University Press. London: H. Milford. 1933. Pp. 103. Price 10s. 6d.

Like Professor Adrian's previous monographs, this is distinguished by clearness and conciseness in description, reasoned analysis of observation and careful distinction between what the author can accept as established and hypotheses or speculations still lacking adequate proof.

The observations on which this work is based were obtained by the oscillograph and amplifiers. An introductory chapter describes the methods employed and discusses the nature of the activity of peripheral nerve-fibres. Subsequent chapters deal with the action of the sense organs, the origin and conduction of impulses which are in consciousness interpreted as pain, the discharges in motor nerve-fibres, and the activity of nerve-cells. Many of his previous conclusions described in "The Basis of Sensation" are restated and when necessary substantiated by further experiments and arguments. Each nervous message consists of a succession of brief waves of surface breakdown in the fibres, and the only gradation of which the message is capable depends on the rapidity with which the waves follow one another. The investigation of the action of sense organs introduces complications, as the question of adaptation, but records of nerve impulses starting in them show how they respond to stimuli. The investigation of pain throws considerable light on the validity of the doctrine of "specific nerve energy", and the general conclusion is stated that the distinctive character of the effects of discharges in the sensory nerves must depend largely on their anatomical distribution in the central nervous system.

These comments can but indicate the scope of the monograph, a study of which is essential to all who wish to obtain even a superficial knowledge of the working of the nervous system.

*The Psychology of Children's Drawings.* By HELGA ENG. Translated by H. STOPFORD HATFIELD. London: Kegan Paul. 1931. Pp. 224. Price 12s. 6d.

This is a well-documented study of the development of a child's drawing from the age of 10 months to 8 years. The first part of the book is descriptive; in the second part the different elements in the drawings are analysed in relation to the mental development of the child and with occasional reference to art, especially of the early Renaissance. In a separate chapter palæolithic and contemporary savage or primitive art is considered in a like connection. The book is thorough and informative without hazardous speculation.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

DECEMBER, 1933.

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BRAIN.

PART 4, VOL. 56.

# POSTURAL RELATIONS OF THE FRONTAL AND MOTOR CORTEX OF THE DOG.[1]

BY CLINTON N. WOOLSEY,
*Department of Anatomy, Johns Hopkins University.*

THE control of posture by the central nervous system has remained the subject of continual study since Sherrington (1896) made his original and stimulating observations on the phenomenon of decerebrate rigidity. A review of the literature (Langworthy, 1928) shows that numerous investigators have sought to determine the centres and pathways responsible for the maintenance of this condition and to discover the source of the influences which normally modify or inhibit it. Such a review makes it evident that the nervous control of posture is a very complex matter involving many levels of the nervous system from the local spinal reflex arc to the cerebral mantle itself. It is the relationship of the cortical level which concerns us here.

Recent studies have offered a conflict of opinion as to the area of the cortex actually involved in postural control. The work of Warner and Olmsted (1923), Olmsted and Logan (1925), King (1927) and Langworthy (1928), supports the view that profound changes of a postural nature, resulting from lesions about the cruciate sulcus in cats, occurred only when the inexcitable area frontalis was destroyed. Lesions limited to the excitable zone produced flaccid paralysis without extensor phenomena. On the other hand Laughton (1928), working with guinea-pigs, rabbits, cats and dogs, McKibben (1929), McKibben and Wheelis (1932) and Bard (1933), using cats, have failed to confirm those results and conclude that extensor rigidity

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[1] This work was done while the author was a Fellow of the Henry Strong Denison Medical Foundation.

and its associated phenomena always follow the destruction of the excitable area itself.

In view of this divergence of opinion it was thought that additional data might confirm the work of one or the other of these groups, or perhaps correlate the views of the two. Since the cat has been used for the major portion of previous studies, a comparative study was projected for the dog, for in that animal's brain the areas with which we are concerned are larger than the homologous regions in the cat. This paper presents the physiological observations made on thirty-two dogs, from which various portions of the frontal and motor areas of the cortex were removed. The evidence obtained supports the thesis that postural phenomena are associated with destruction of the excitable area of the cortex. A study of the cyto-architecture of the areas ablated and of the degenerations produced by certain of the lesions will form the subject of a later report.

## METHODS.

The experiments were controlled not only by a preliminary histological study of the cortex, but also by delimitation of the excitable area with a unipolar electrode. This electrode carried either induced current from a secondary coil, or a 60-cycle alternating current from the house circuit reduced to voltage values variable between 2 and 5 volts.

Operations were performed aseptically under full surgical anæsthesia induced either with ether by inhalation or with nembutal (Abbott) given intra-peritoneally. 25 to 40 mgm. of the latter drug per kilogram of body-weight gave surgical anæsthesia lasting from two to four hours with a threshold of electrical stimulation lower than occurred under ether. (*Cf.* Keller and Fulton, 1931; Fulton and Keller, 1932.)

The animals were kept under observation after operation for periods of time varying from a few weeks to several months. Then they were killed by anæsthetics and the brains fixed with 10 per cent. formalin injected through the heart, preceded by warm normal saline to wash out the vessels. The extent of the actual lesion in each case was carefully determined after removal of the brain from the skull.

## EXPERIMENTAL OBSERVATIONS.

### *I.—The Extent of the Electrically Excitable Cortex of the Dog.*

Electrical stimulation showed that the excitable motor area was localized to the lateral third of the anterior and the whole of the posterior sigmoid gyrus (fig. 1).. The gyrus proreus and the medial half to two-thirds of the anterior sigmoid were found to be silent; so also was the cortex lateral to the coronal fissure.

Well-defined movements of the contralateral facial muscles were obtained upon stimulating points of the cortex in the outer third of the anterior sigmoid. Excitation of the anterior gyrus as it began to swing around the end of the cruciate sulcus produced contralateral flexion of the neck. As the exploration was carried to the posterior gyrus isolated flexor movements of the fore-leg appeared, usually of the whole limb but sometimes of its segments. Occasionally movements of extension occurred. When about one-third of the length of the posterior gyrus had been traversed, stimuli produced simultaneous flexion of the fore- and the hind-leg. From the medial half, together with the medial surface of the posterior sigmoid, movements of the hind-leg were obtained.

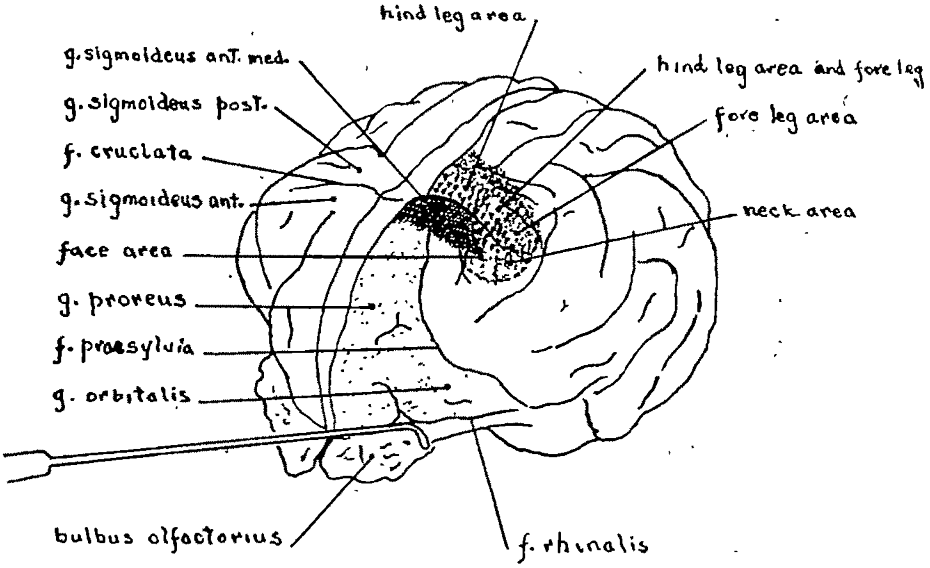


FIG. 1.—Drawing of fore-brain of the dog, after a photograph, showing the excitable area, the histological fields about the cruciate sulcus, and the extent of the inexcitable frontal area. The Betz-cell area is indicated by small triangles; granular cortex by fine stippling; agranular cortex is cross-hatched.

Examination of both hemispheres in the same animals showed no appreciable variation in the distribution of cortical motor points.

If the strength of stimulus was properly controlled no reaction resulted when areas outside those just described were stimulated. However, if, after exciting a point in the motor area, another lying within a short distance but outside the excitable area were stimulated, the phenomenon of facilitation could be demonstrated.

Histological study showed that the area responding to electrical stimuli extended beyond the distribution of the typical Betz-cells to overlap the sensory granular cortex posteriorly and an agranular type, similar to Brodmann's Area 6, anteriorly. This is important to bear in mind in drawing conclusions from the ablation experiments.

### *II.—The Effects of Ablations in the Frontal and Motor Areas.*

As a result of differential ablations it was found that lesions located entirely anterior to the electrically excitable area produced no demonstrable effects, but as the excitable zone became involved alterations began to appear which reached a maximum when the entire responsive area was destroyed. It will be convenient first to indicate the experiments which led to this conclusion, and then to describe in some detail the results of effective cortical ablations.

TABLE I.

| Animal number | Extent of lesion |
|---|---|
| 1. | G. proreus and adjacent medial surface, L. |
| 2. | ,, ,, ,, ,, ,, ,, ,, |
| 3. | ,, ,, ,, ,, ,, ,, Bilat. |
| 4. | ,, ,, ,, ,, ,, ,, ,, |
| 5. | G. proreus and coronal tip, L. |
| 6. | ,, ,, ,, ,, ,, Bilat. |
| 7. | G. proreus, adj. med. surface, g. orbitalis, L. |
| 8. | ,, ,, ,, ,, ,, ,, ,, ,, |
| 9. | 1st op., g. proreus, adj. med. surface, g. orbitalis, L.<br>2nd op., g. proreus, g. sigmoid., R. |
| 10. | 1st op., g. proreus, adj. med. surface, g. orbitalis, L.<br>2nd op., g. sigmoid., Bilat. |
| 11. | G. proreus, adj. med. surface, g. orbitalis, Bilat. |
| 12. | G. proreus (upper one-third), Bilat. |
| 13. | G. proreus, coronal tip, g. sigmoid. ant., Bilat. |
| 14. | ,, ,, ,, ,, ,, ,, ,, ,, |
| 15. | ,, ,, ,, ,, ,, ,, ,, ,, |
| 16. | ,, ,, ,, ,, ,, ,, ,, ,, |
| 17. | ,, ,, ,, ,, ,, ,, ,, L. |
| 18. | 1st op., g. sigmoid., L.<br>2nd op., g. proreus, g. sigmoid., R. |
| 19. | G. sigmoid., L. |
| 20. | ,, ,, ,, |
| 21. | G. sigmoid, ant. (med. two-thirds), L. |
| 22. | G. sigmoid, ant. (med. one-half), and adj. med. surface, L. |
| 23. | ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, |
| 24. | 1st op., g. sigmoid. ant. (med. one-half), and adj. med surface, L.<br>2nd op., g. sigmoid. ant. (lat. one-half), g. sigmoid. post. (lat. two-thirds), R. |
| 25. | 1st op., g. sigmoid. ant. (med. one-half), adj. med. surface, Bilat.<br>2nd op., g. sigmoid. ant. (lat. one-half), g. sigmoid. post. (lat. one-half), L. |
| 26. | G. sigmoid. ant. (lat. one-half), g. sigmoid. post., L. |
| 27. | ,, ,, ,, ,, ,, ,, ,, ,, ,, |
| 28. | ,, ,, ,, ,, ,, ,, ,, ,, ,, |
| 29. | ,, ,, ,, ,, ,, ,, ,, ,, ,, |
| 30. | ,, ,, ,, ,, ,, ,, ,, ,, ,, |
| 31. | G. sigmoid. post., L. |
| 32. | ,, ,, ,, and a portion of sensory cortex, L. |

(1) *Lesions of frontal areas anterior to excitable cortex.*—By reference to fig. 1 and Table I, the situation and extent of the lesion in each animal can be determined. The region anterior to the sigmoid gyrus includes (1) that portion of the coronal gyrus lying anterior to the sigmoid gyrus above the presylvian fissure, which may be conveniently designated the coronal tip; (2) the gyrus proreus down to the olfactory bulb, together with the adjoining medial surface; and (3) the orbital gyrus which extends infralaterally between the presylvian and rhinal fissures. Lesions of various extent were made in this region in 12 animals (1-12), unilaterally in 7, bilaterally in 5. Negative results were obtained in each case, except for an increase in general motor activity in 3 and 5. This type of alteration was seen in other animals (*vide infra*, 15, 10, 27). Since its occurrence bore no constant relation to the site of the lesion the explanation for it seems to lie rather in technical procedures, although this cannot be proved.

(2) *Lesions of anterior areas encroaching upon excitable cortex.*—In five animals (13-17) lesions of the anterior areas extended backward to involve almost completely the anterior limb of the sigmoid gyrus. Four of these cases were bilateral, the other was a unilateral ablation. No sensory or motor symptoms occurred in the first three animals except for a rather marked hyperactivity in 15. Dogs 16 and 17, however, presented distinct sensory and motor disturbances, consisting of altered sensitivity to pin prick, uncorrected postures of the legs, extensor rigidity and difficulty in the use of the limbs. Considerable hæmorrhage occurred at operation in 17 and this animal showed gross contralateral weakness for the first half week. Symptoms persisted in 16 until the animal was sacrificed (four weeks), but in 17 they disappeared after one month. In the latter case the posterior sigmoid in its middle portion was involved in adhesions.

(3) *Lesions destroying the entire sigmoid gyrus.*—In five cases the entire sigmoid gyrus was removed with striking results. In animal 9, which previously had had the left gyrus proreus and the orbital gyrus removed without effect, a right-sided lesion was made which included the gyrus proreus and the entire sigmoid gyrus. In 18, 19 and 20 the lesions were limited to the sigmoid gyrus on the left. After one week the gyrus proreus and the gyrus sigmoideus were removed from the right hemisphere of 18. The sigmoid gyrus of dog 10, from which the left gyrus proreus and the gyrus orbitalis had been removed earlier (*vide supra*), was destroyed bilaterally. Maximal changes, which will be considered in detail below, occurred in these animals. Two of the

animals (19 and 20) showed rather marked contralateral weakness for the first few days after the operation. Since these were the only two cases, except for 17, which showed this degree of weakness, it may be well to remark that in all three of these animals bleeding was considerably greater than in any others of the whole series.

(4) *Partial ablations of the sigmoid gyrus : (a) Lesion of the anterior sigmoid.*—Partial ablations of the sigmoid gyrus were next undertaken to determine what portion of it was responsible for the clinical phenomena produced. The evidence already obtained indicated that the anterior sigmoid could be destroyed almost completely without effect, though this was not true in all cases. Therefore the left anterior sigmoid alone was removed from one animal (22). No response to electrical stimulation was obtained except at the very lateral end of the gyrus and this part was not included in the lesion. Very mild symptoms lasting three weeks followed this ablation. At autopsy about two-thirds of the posterior sigmoid gyrus was found elevated and roughened by adhesions.

(*b*) *Lesions of the medial half of the anterior sigmoid.*—In four animals the medial half of the anterior sigmoid, together with the adjacent medial surface, was carefully destroyed. This was done with minimal hæmorrhage since it was not necessary to sever any large blood-vessel. In three of the cases (22, 23 and 24) the lesion was limited to the left side; in the fourth (25) it was bilateral. None of these animals ever developed any signs of sensory or of motor defect, although they were subjected to detailed examination repeatedly.

(*c*) *Subsequent lesions of the excitable cortex in animals of group* (*b*).—In two of these cases subsequent lesions of the electrically excitable area were made. The lateral third of the anterior and the lateral two-thirds of the posterior sigmoid were removed from the right hemisphere of 24. The lateral halves of the left anterior and posterior sigmoid were destroyed in 25. Typical alterations occurred after these lesions, though they were not as severe as in the total destruction of this gyrus. Furthermore, in 25 the resulting physiological changes affected chiefly the contralateral fore-leg—a finding in consonance with the fact that the cortical area of the hind-leg was left intact.

(*d*) *Lesions of the excitable cortex alone.*—From five animals (26-30) the electrically excitable area was removed by destroying the lateral half of the anterior and the whole of the posterior sigmoid gyrus. Each of these dogs developed in a pronounced manner the same clinical features which characterized those animals from which the entire sigmoid gyrus was excised. Not one of them showed a flaccid paralysis. Every one of these animals could stand, walk and even run as soon as the effect of the anæsthesia (ether) wore off.

(*e*) *Lesions of the posterior sigmoid.*—Practically the same effects were produced by destroying the entire posterior sigmoid alone in one case (31), and the posterior sigmoid plus a portion of the cortex directly behind it in another (32.)

From these experiments it is evident that lesions entirely anterior to the electrically excitable area were not associated with the appearance of clinical manifestations, but that symptoms did appear when the excitable area became involved and were maximal when the entire responsive area was destroyed. The typical alterations produced by effective lesions will now be described.

Many deviations from the normal were found in these animals, both when they were observed during spontaneous activity and when they were subjected to special test performances. Changes were always contralateral to the lesions and were easily demonstrable in unilateral cases by comparison with the unaffected side. Marked weakness occurred in but three cases, as noted. All others could stand, walk, or even run as soon as the anæsthesia wore off. Stiffness of the affected limbs was noted in some animals, but usually progression was fairly normal except for moderate inco-ordination. Footing was insecure on a smooth surface, so that slipping frequently, but falling seldom, occurred. Paws often were left dorsum to the ground, and limbs assumed abnormal postures of adduction, abduction, ante- and retro-position. Similarly, such positions might be passively imposed and remain uncorrected until some spontaneous activity required the use of the part. Animals accustomed to climbing stairs had difficulty in doing so after operation through failure of the affected limbs to clear the steps readily.

In all cases well-marked contralateral extensor rigidity was easily demonstrable. This became evident when the animal was lifted in a horizontal position above the floor, and was best seen when a hammock was used for support (Plate XII, figs. 2 and 3). For while the ipsilateral limbs flexed, rigid extension engaged both contralateral legs at all joints, including ankle and wrist, and the toes fanned. Passive flexion was resisted, and during the first week post-operatively there resulted a spring-like rebound when the foot was released after passive flexion of the wrist. The limb as a whole gave way with "jack-knife" suddenness to pressure applied at the sole. Rigidity was likewise apparent when the animal was held back-to-examiner (figs. 4, 5, 6). In either the ventral or the vertical position the fore- and the hind-legs seemed equally hypertonic, but when the animal was placed on its back the fore-leg alone was usually affected (fig. 12). In some cases spontaneous extension did not occur at all in the dorsal position, or, if it did, the limbs flexed when the animal became quite quiet. However, a difference in the extensibility of the limbs of the two sides could be demonstrated by gently pushing the hind-legs caudalward with pressure applied just above the knees, or by forcing the fore-legs forward by pressing just above the elbows. All four limbs were thus passively extended, but the angle through which one had to move the limbs to produce extension was much less on the affected side than on the unaffected one (fig. 13). The difference in rigidity could also be demonstrated by grasping the animal about the thorax and gently swinging it so that a pendular movement was imparted to the limbs, particularly the fore-limbs. The ipsilateral fore-leg alternately flexed and extended at all joints, including the wrist, as the limb swung backward and forward respectively. The contralateral one, however, moved as a rigidly extended whole, and flexion failed to occur.

In most of the cases a further feature was evident when the animal was held in the back-to-examiner position. There was extreme flexion of the animal's neck and trunk to the contralateral side and slightly forward (fig. 11). If an attempt were made to correct this position by straightening the body a marked resistance was encountered. This hypertonicity of the trunk muscles was emphasized by holding the animal in a lateral position with the side parallel to the ground. A normal animal attempts to right itself and produces a concavity of the body upward, whichever side be held toward the ground. But in these animals, when the side contralateral to the lesion was toward the floor, there was a marked concavity downward (fig. 10), and when the contralateral side was up the normal upward concavity was greatly accentuated (fig. 9). Hypertonicity and resistance to lengthening of the trunk musculature have not previously been described in association with experimental cortical lesions.

Typical difficulties were noted in the animals' ability to use their limbs. These were especially evident in the usual escape efforts which are made when an animal is held. Immediately after operation only the ipsilateral limbs took part in these movements; the contralateral ones remained quite still. A few days later attempts at movement were made on that side, but the limbs tended to move as rigid wholes from the proximal joints. Although improvement occurred, the difficulty continued for months. This "paralysis" of movement was well shown when the animal tried to get out of the hammock (fig. 8). The ipsilateral limbs were readily extracted from the holes through which the legs passed, but the contralateral ones could be withdrawn only with the assistance of the ipsilateral members. This inability to extricate the limbs and place them beside the body is a failure of one of the placing reactions of Rademaker (1931) and Bard (1933). Investigation revealed that other placing reactions were also absent. Thus when the non-blindfolded animal was moved toward a table edge, a visual placing reaction was elicited as soon as the dog was near enough to place the foot upon the table (fig. 16). Only the ipsilateral one was so placed. If the animal was prevented from seeing the table and the backs of the fore- or hind-paws were touched to the edge the ipsilateral limb at once was placed upon the table (figs. 17, 18, 20, 21). The contralateral one failed to react until backward displacement by pressure against the table supplied an added stimulus. Likewise after the chin was brought in contact with the underlying surface while the fore-legs were held down, only the ipsilateral paw was placed beside the jaw when the limbs were released (fig. 19).

Other differences, comparable to the disturbances of the hopping reactions seen after similar lesions in cats (Bard), were noted in the use of the legs in all cases. When a normal dog is made to stand erect on its hind feet it steps back with both legs to correct to the all-fours position. After the excitable area had been destroyed on one side the contralateral limb failed to show this reaction; the ipsilateral one alone stepped back with a tendency to execute a circle about the other foot, which remained firmly stationed as a pivot. If instead of being held in one position, the dog were caused to walk forward in the erect attitude the ipsilateral leg stepped in a normal manner; the contralateral one dragged along in hemiplegic fashion, usually with toes turned under, or at times it would move with infrequent, reluctant steps. Likewise the contralateral limb failed to correct its position upon lateral displacement of the body (fig. 24).

Similar defects were demonstrated in the fore-leg by causing these dogs to walk on the fore-legs alone. The normal one stepped readily; the affected one did not, with the result that pivoting occurred about the contralateral foot. When the animal walked backward on its front legs the normal limb performed stepping movements; the abnormal one failed to do so and slid medially toward the ipsilateral side (fig. 14).

One other reaction may be noted here. If, while standing on all four legs, one of these animals was lifted off the floor, even though great care was taken to lift the animal evenly as a whole, the contralateral feet left the floor before the ipsilateral ones did, and became elevated above it an inch to an inch and a half before the ipsilateral ones left it (fig. 22). In returning, the ipsilateral feet were the first to touch the surface, as if reaching out for it.

Crossed extension reflexes could be elicited readily from the contralateral fore and hind limbs by a painful stimulus, or pressure to the corresponding foot pad, or by passive movement of the whole normal limb. Repeated passive flexion and extension of the ipsilateral leg often resulted in a gradual increase of extensor tone in the contralateral limb which finally produced a rigidly extended extremity (fig. 15).

The contralateral tendon-jerks were hyperactive, and alterations in the normal reactions to stimuli of deep pressure and of prick were also found on the side opposite to the lesion.

The clinical condition of the animals improved with the passage of time. But even months later all changes could be demonstrated in a a lessened degree. The photographs of animal 30 were taken two months after operation. The same phenomena were equally present when the dog was sacrificed two and one-half months later. In other cases this was true when they were killed seven months after operation. In some, however, reactions were nearly normal after two months. The hopping reactions apparently recovered most, but there was also a decrease in the extensor rigidity. The extensor attitude persisted; the resistance to passive flexion tended to disappear.

## DISCUSSION.

It has been possible in chronic experiments on dogs to show a correlation between the destruction of the excitable motor cortex of this animal and the occurrence of certain clinical phenomena of a postural nature. The excitable cortex was outlined by electrical stimulation. Lesions entirely anterior to this area failed to produce alterations in the sensori-motor reactions of the animals; but as the motor cortex became involved disturbances began to appear which became maximal when the entire excitable area was removed. The alterations were no greater when the motor area and all cortex anterior to it were destroyed than when the motor area alone was ablated.

The motor cortex of the dog, as outlined by electrical stimulation, is limited to the lateral third of the anterior sigmoid and the whole length of the posterior sigmoid gyrus, together with its medial extension for about two-thirds the width of the gyrus. This tends to agree with the initial findings of Fritsch and Hitzig (1870). Slightly more of the anterior sigmoid responded to stimulation than gave origin to the cortico-spinal tracts in the dog studied by Holmes and May (1909). Our experience indicates that in the dog there is an orderly representation of contralateral movements from the face, through the neck and fore-leg to trunk and hind-leg, beginning in the outer third of the anterior sigmoid and continuing around the end of the cruciate sulcus to include the entire posterior gyrus. This agrees with the findings of Smith (1933) which have just been reported. There is no evidence in the dog of centres for the facial and neck musculature in the gyrus proreus corresponding to the findings of McKibben and Wheelis (1932) for the cat, which also are not supported by Langworthy's histological studies. The position of the face centre in the dog corresponds approximately with that reported for the cat by Weed and Langworthy (1926). The hind-leg areas of these two animals also correspond. But the fore-leg centre of the dog occupies a lateral position in the posterior sigmoid corresponding to their area D, which was inexcitable and did not have, in the cat, the characteristic structure of motor cortex. In the cat the fore-leg centres are medial to the face centres in the anterior sigmoid (Weed and Langworthy, 1926; Langworthy, 1928).

Unilateral destruction of the excitable motor area of the dog gave the following clinical phenomena: (1) The contralateral limbs assumed extended postures when the animal was held off the floor, suspended in a hammock or held with back to the examiner, and there was resistance to passive flexion in the extended limb. Rigidity might also be demonstrated, especially in the fore-leg, when the animal was on its back. (2) A similar hypertonicity affected the contralateral trunk musculature, resulting in a concavity of the body to that side when the animal was held in test positions, and there was resistance to passive straightening. (3) Weakness and inco-ordination affected the contralateral side. Usually the weakness did not amount to flaccid paralysis and the animal could stand, walk or run immediately after emerging from the anæsthesia. (4) Abnormal positions of the feet and limbs occurred spontaneously or might be passively imposed. These were not corrected until spontaneous movement required the use of the part. (5) There was failure to use the contralateral limbs in such movements as efforts to escape and in stepping backwards when held erect on the hind legs. Examination of these difficulties revealed that the hopping and placing reactions were deficient. (6) When the animal was lifted off the floor the contralateral limbs left first. (7) Crossed extension reflexes occurred in the contralateral limbs to stimuli applied to the ipsilateral members. (8) The contralateral tendon reflexes were hyperactive. (9) There was impairment of superficial and deep sensibility.

All these alterations occurred contralaterally to the lesion and in no animal was the ipsilateral side affected. They were greatest immediately after operation and gradually decreased in severity until after several weeks many animals seemed quite normal. In others the deficiencies continued for months.

It is evident that the occurrence of extensor rigidity in association with lesions of the motor cortex does not agree with the view, derived from experiments on cats, that destruction of the area frontalis produces this effect. Clinically it is well known that rigidity occurs in association with pyramidal tract lesions in man. The similarity of hemiplegic spasticity to decerebrate rigidity has been stressed by Walshe (1919, 1923, 1929), who believes that the two conditions are physiologically identical although the former is but a fractional expression of the latter. This analogy was noted also by Riddoch and Buzzard (1922). However, the fact that capsular lesions produce greater spasticity than cortical motor lesions has suggested (Walshe 1919) that something more may be involved in the former than mere interruption of the pyramidal fibres. Actually it may mean a more complete lesion of the cortico-spinal fibres in the capsule or the interception of additional pathways. Those who hold that destruction of the area frontalis is responsible for the appearance of rigidity deny that the pyramidal tract plays any part. In this connection and confirmatory of the results presented here, it is interesting to note that Ranson, Muir and Zeiss (1932) studied the occurrence of extensor rigidity following spinal cord lesions in cats and concluded that in this animal, as in man, the cortico-spinal tracts convey impulses which inhibit extensor tonus. This has been confirmed for the dog and the cat by Tower (unpublished) who sectioned the pyramid from the ventral surface. Langworthy (1928) on the other hand sectioned the decussation of the pyramids in the sagittal plane from above and obtained flaccid paresis.

The premotor area of the hemisphere entered as a factor for consideration in tone distribution with the observations of Wilson and Walshe (1914) on "tonic innervation," of Adie and Critchley (1927) and of Critchley (1930) on forced grasping and groping in association with tumours and vascular lesions of this area. But how these disturbances may be related to what is usually thought of as pyramidal spasticity is not clear. Forced grasping and groping in man disappear when the cortico-spinal tracts become completely involved and spasticity is maximal.

Richter and Hines (1932) were able to reproduce experimentally "forced" grasping in monkeys by removing Brodmann's Area 6. They were unable to demonstrate any associated spasticity. Study of the relationship of Areas 4 and 6 in monkeys (Fulton, Jacobsen and Kennard, 1932) showed that forced grasping without spasticity occurred after lesions of Area 6, and that flaccid paralysis resulted when Area 4 was destroyed. A combined lesion of the two however (Fulton and Kennard, 1933) produced the grasp reflex with marked spasticity, showing that unlike the situation reported for man the grasp reflex was not abolished by destruction of the motor cortex, and suggesting that for the appearance of spasticity the lesion must affect Areas 4 and 6 simultaneously.

In man circumscribed lesions of the Betz-cell area have not been made. The nearest approach was that of Horsley (1909) who removed all the cortex of the precentral gyrus from which electrical excitation produced movements in the corresponding arm. Our present knowledge of the structure (Brodmann, 1909; Vogt and Vogt, 1919; Economo and Koskinas 1925), and the excitability (Foerster, 1931) of this portion of the cortex makes it certain that the lesion Horsley produced included not only Area 4 but also Area 6. It would be important to know if a lesion of Area 4 alone would produce the same spasticity.

What have we learned in dogs of the relation of cortical areas to the occurrence of spasticity? It has not been possible to confirm the view that spasticity results when the inexcitable frontal areas are destroyed. Lesions of this region in the dog produced no effect. On the other hand when the excitable zone became involved symptoms began to appear which were maximal when the entire stimulable cortex was removed. A solution of the difficulty of correlating the findings of various workers may lie ultimately in a further analysis of the excitable area. For the motor cortex as outlined electrically in the dog extends beyond the distribution of the Betz-cells. In the frontal lobe of the dog studied histologically the medial third to half of the anterior sigmoid gyrus, which is not electrically excitable, is characterized by an agranular type of cyto-architecture similar to Brodmann's Area 6, while all the remainder of the frontal lobe of the dog's cortex is of the typical granular variety. Further, although the remainder of the anterior sigmoid gyrus and the whole of the posterior sigmoid gyrus are susceptible to electrical stimulation with low current strengths, the total areas do not possess the typical cyto-architecture of the motor cortex. In the anterior sigmoid gyrus a short distance anterior to the crest of the cruciate sulcus the cortex is similar to Brodmann's Area 6, while the posterior division of the posterior sigmoid gyrus is characterized by the appearance of layer IV. However, in the depth of the cruciate sulcus, with the exception of the medial non-excitable cortex of the anterior sigmoid and of that forming the wall of the most lateral part of the posterior, the cortical mantle contains the large pyramidal cells of Betz in the fifth layer.

Although the experiments reported in this paper have taken cognizance of the cyto-architecture of the non-excitable medial division of the anterior sigmoid, it is practically impossible to differentiate previous to experimental ablation the exact limit of the motor cortex anteriorly in the anterior sigmoid and posteriorly in the posterior sigmoid, because the excitable area overlaps slightly the agranular Area 6 anteriorly and the granular area posteriorly. However, since most of Area 6 was destroyed by lesions of the medial half of the anterior sigmoid gyrus without effect, and since the same area was left intact with the production of maximal effects, it seems that Brodmann's Area 6 can have little to do with the production of spasticity in the dog. It, therefore, appears that cortical rigidity in this animal is a release phenomenon from the true Betz-cell area.

Extensor rigidity is but one of the manifestations of lesions destroying the excitable cortex of the dog. The question arises as to what relation the rigidity may have to these other disturbances. We may note that no one has described the occurrence of rigidity "in pure culture." Langworthy observed uncorrected postures of the legs, failure of the limbs to take part in escape efforts and alterations in superficial and deep sensitivity. He felt that these difficulties in postural adjustment and heightened threshold to sensory stimuli could well be explained on a basis of the rigidity. Bard, in his study of abnormalities of posture after lesions of the sensori-motor area in cats, came to the conclusion that the difficulties of adjustment were due to deficient hopping and placing reactions. He raised the question as to whether or not the rigidity might explain the difficulties, and decided in favour of the negative. For the rigidity was found to vary and at times was absent, while the deficiency of the placing and hopping reactions remained unchanged. Moreover, Brooks (1933) found in the rat that these reactions were disturbed without the appearance of rigidity.

There are still two conceptions possible regarding the relationship of the rigidity to the associated phenomena. Either there is no causal connection and each is due to the destruction of separately functioning structures, or both result when the reflexes mediated through the destroyed centres are lost. As to the former, we may simply say that the separation has not yet been made. The view suggested here is that the rigidity appears because the reflex mechanisms of this level have been abolished.

Since many of the associated phenomena, such as the failure to correct abnormal postures or to respond properly to nociceptive stimuli, are distinctly of a sensory defect character, the sensory element must be considered. Whether these are actually the effect of sensory lesions or merely result from destruction of the efferent arc would be difficult to say. That all the symptoms may be due to a pure motor lesion is supported by experimental evidence that the entire symptomatology, as described in this paper, can be produced in cats and dogs by section of the pyramid in the medulla from the ventral surface (Tower, unpublished). However, Dusser de Barenne (1916) has shown for the cat that the sensory area overlaps the motor. This seems to be true for the dog also (Brown, unpublished), as was held by earlier workers on the cortex of this animal (Luciani, 1915). If these facts are true, it is impossible to destroy selectively either the motor or sensory area in these animals. Even in man Horsley (1909) found that sensory, particularly proprioceptive, changes occurred after destruction of the motor arm area. And in the macaque Dusser de Barenne (1924) showed a similar overlap.

It is therefore necessary to think of these experimental "motor" lesions as a combination of sensory and motor elements, and of their effects as losses of reflexes which pass through the centres destroyed. The difficulties of correcting posture are true defect phenomena. The rigidity, however, is a positive manifestation due to release of lower centres from cortical control. This control is not exercised by separate but by the same cortical centres that are involved in carrying out the reflexes which have been lost.

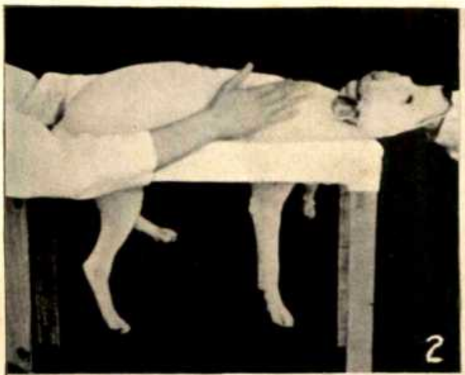
It is probable that in decerebrate rigidity there is a release of lower centres from several inhibitory centres of which the motor cortex, or the sensori-motor cortex, is but one. This view has been stressed in the recent papers of Ranson and his colleagues who have been able to show various degrees of rigidity according to the level of transection of the brain-stem (Ranson and Hinsey, 1929A; Hinsey, Ranson, McNattin, 1930; Windle, 1929). Can a general correlation be made between the occurrence of rigidity and the destruction of centres which normally permit the animal to adjust itself to its environment through movements of righting, progression, placing and hopping, and the like? The evidence is by no means conclusive, but it is suggestive of such a possibility. Such an interpretation is consistent with, and indeed, suggested by, the conception already current concerning decerebrate rigidity and its relation to progression. Movement and the extensor attitude are reciprocal phenomena. The latter is inhibited during movement and appears, when the tone-maintaining centres are still intact, after the mechanisms presiding over movement have been destroyed.

## SUMMARY.

From thirty-two dogs various areas of the motor and frontal cortex, controlled histologically and by electrical stimulation, were removed. The animals were studied for periods varying from a few weeks to several months. Lesions entirely anterior to the excitable area failed to produce effects. As the excitable area became involved symptoms appeared which were maximal when this area alone was ablated. These changes were entirely contralateral and consisted of extensor rigidity and resistance to passive flexion in the legs; a similar hypertonicity of the trunk musculature resulting in concavity to that side with resistance to passive straightening; uncorrected postures of the extremities; failure of placing and hopping reactions; crossed extension reflexes; hyperactive tendon reflexes; decreased superficial and deep sensitivity. There was no true flaccid paralysis.

The total area susceptible to electrical stimulation did not possess the typical structure of motor cortex. Anteriorly it overlapped an area similar to Brodmann's Area 6. Posteriorly layer IV appeared. The evidence indicates that removal of Area 6 does not produce spasticity in the dog. Rather rigidity results when the motor or sensori-motor area is destroyed.

PLATE XII.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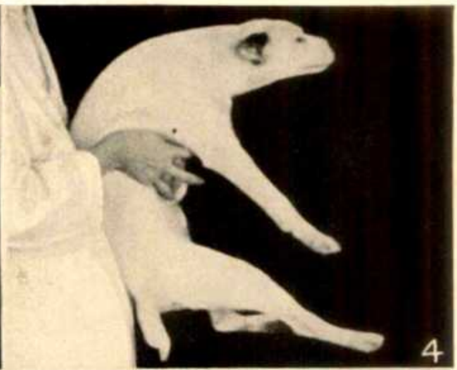
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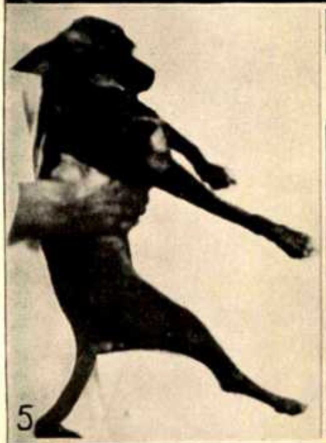
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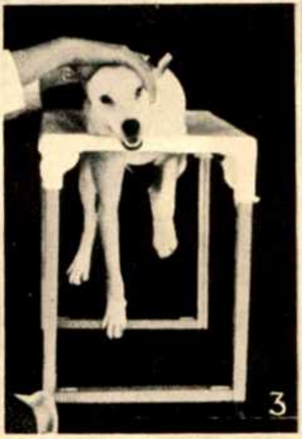
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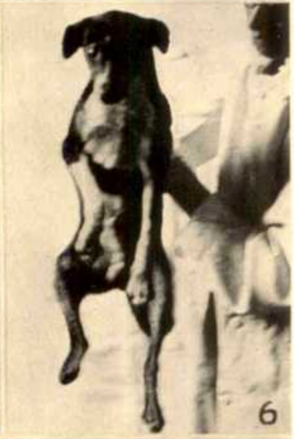
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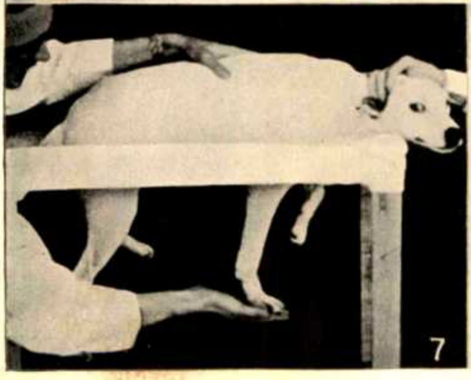
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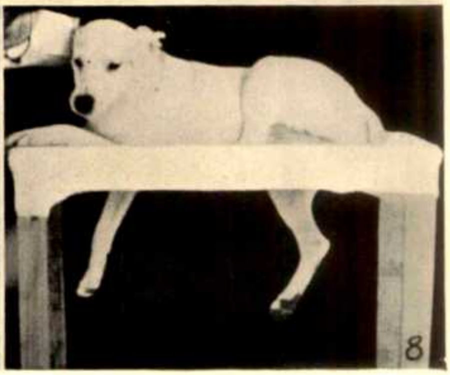
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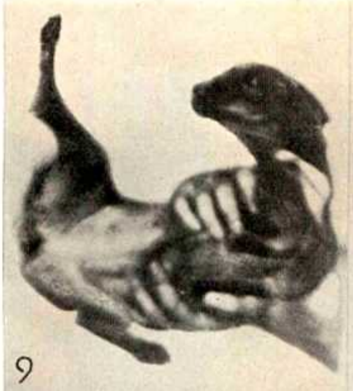
*To illustrate paper by Clinton N. Woolsey.*

PLATE XIII.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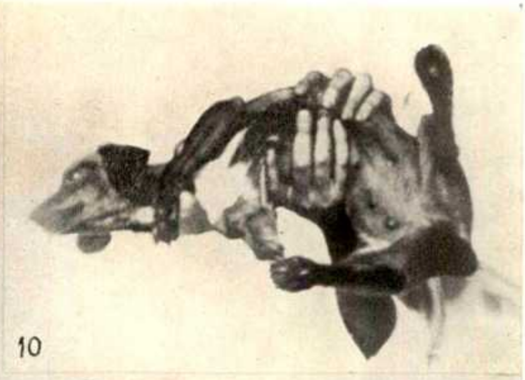
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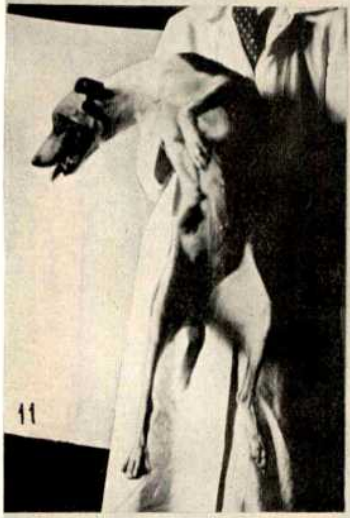
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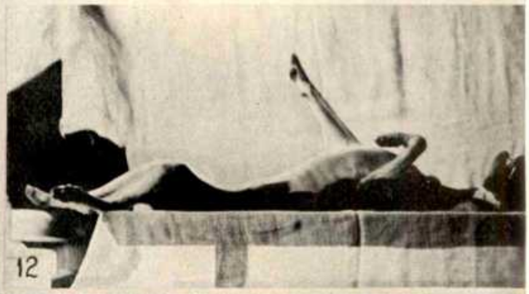
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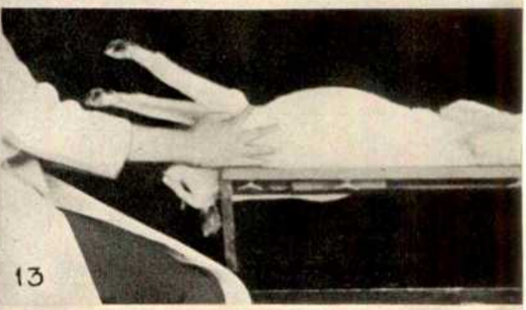
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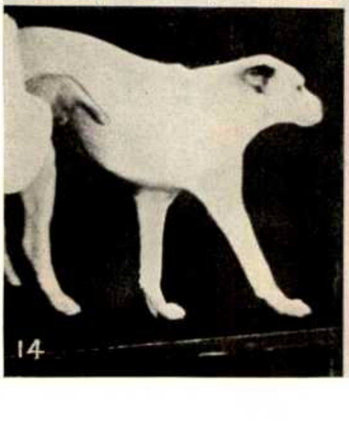
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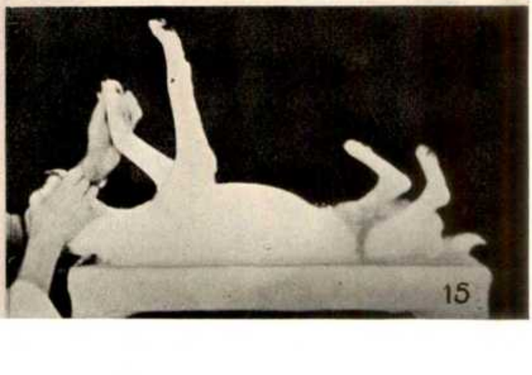
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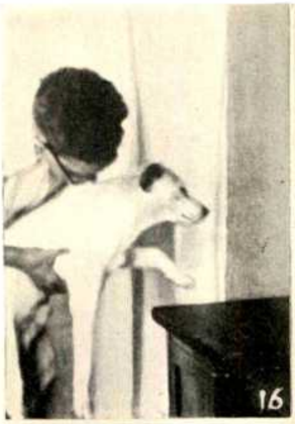
PLATE XIV.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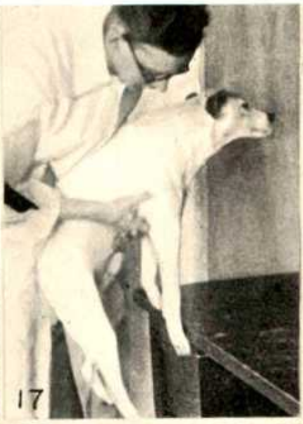
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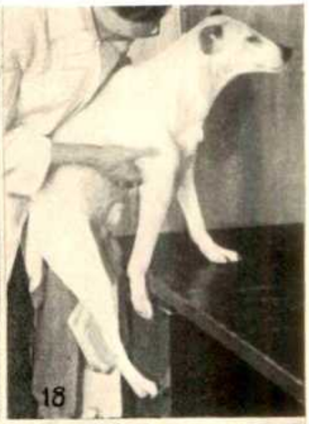
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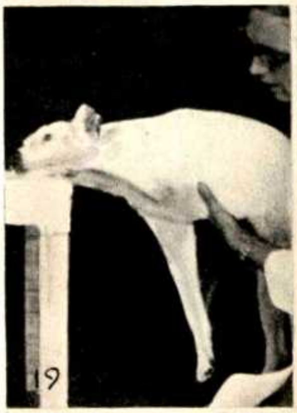
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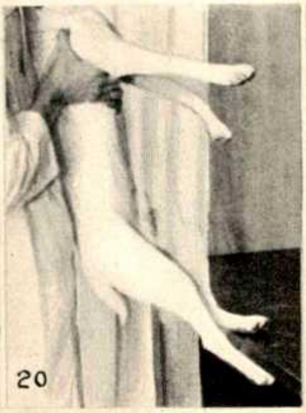
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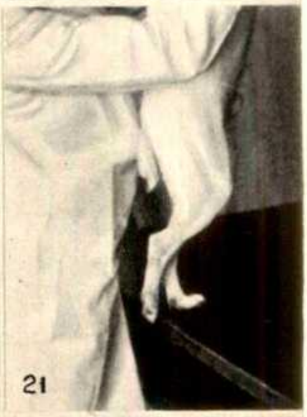
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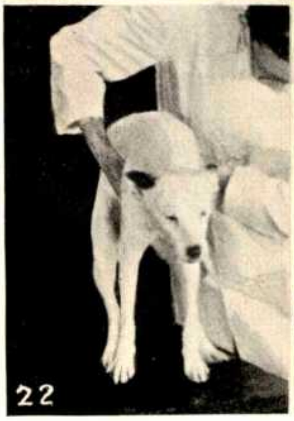
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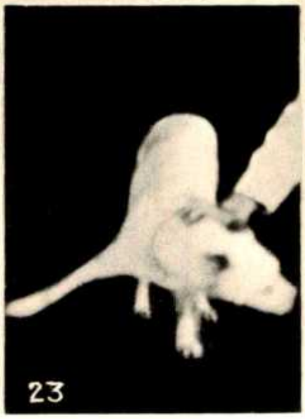
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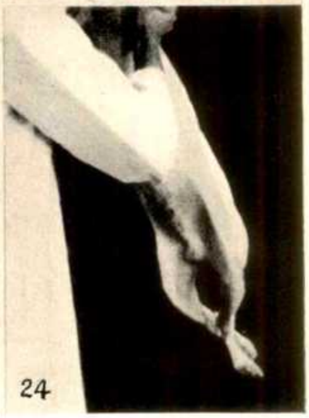
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*To illustrate paper by Clinton N. Woolsey.*

## PLATE XII.

FIG. 2.—Dog 30, photographed two months after removal of the left excitable cortex, showing extensor rigidity of the contralateral limbs and flexion of the ipsilateral ones while suspended in a hammock.

FIG. 3.—Same, from in front. Note fanning of toes of extended limbs.

FIG. 4.—Same animal, held back-to-examiner.

FIG. 5.—Dog 26, photographed two weeks after removal of the left excitable cortex, showing contralateral extensor rigidity.

FIG. 6.—Dog 10, from which the left gyrus proreus and left orbital gyrus were removed first without effect, photographed four months after a second operation at which the right sigmoid gyrus and gyrus proreus were ablated. Typical extension is seen in the limbs contralateral to the sigmoid lesion.

FIG. 7.—Dog 30, showing increased resistance to pressure on the sole.

FIG. 8.—Dog 30, illustrating the manner in which the ipsilateral limbs are used normally to escape from the hammock, while the contralateral limbs remain extended and exhibit deficient placing reactions.

## PLATE XIII.

FIGS. 9 and 10 —Dog 26, photographed two weeks after removal of the left excitable area. When the side contralateral to the lesion is uppermost there is an accentuation of the normal upward concavity of the body. When the contralateral side is down the concavity is downward. The trunk musculature of the contralateral side is hypertonic and resists passive straightening of the body axis.

FIG. 11.—Dog 20, from which the left sigmoid gyrus was removed. There is extensor rigidity of the right limbs. The neck and shoulders are acutely flexed to the contralateral side by the hypertonic musculature.

FIG. 12.—Same animal, lying quietly on its back, showing extensor rigidity of the contralateral fore-leg.

FIG. 13.—Dog 30, illustrating the difference in readiness of the limbs to extend when pressure is applied above the elbow. Both have just become extended. The contralateral limb traversed the lesser angle. The difference is often much more marked.

FIG. 14.—Dog 30, made to walk backwards on the fore-legs. The ipsilateral limb executes stepping movements; the contralataral (right) one drags.

FIG. 15.—Dog 30, on its back, illustrating crossed extension reflex. This animal did not show extensor rigidity spontaneously in this position.

## PLATE XIV.

FIG. 16.—Dog 30, illustrating the visual placing reaction of the fore-leg. The contralateral limb fails to place, remaining rigidly extended.

FIG. 17.—Same animal. The backs of both fore paws were simultaneously touched to the table edge. The ipsilateral foot is being lifted; the contralateral one does not react.

FIG. 18.—The ipsilateral foot has been placed upon the table. The contralateral leg has been over-extended by pressure against the table edge. At this point the right foot was raised and placed upon the table also.

FIG. 19.—Both fore-legs were held down while the chin was brought into contact with the underlying surface. Upon release of both limbs only the ipsilateral one was placed beside the jaw.

FIGS. 20 and 21 show for the hind-legs what figs. 17 and 18 do for the fore-legs.

FIG. 22.—When the animal was lifted off the table the contralateral feet left first. The difference was usually more marked.

FIG. 23.—The animal was pushed toward the contralateral side. Instead of effectively correcting for the displacement or maintaining its footing the left leg slipped from under the animal.

FIG. 24.—The contralateral hind-limb failed to correct its position when the body was moved lateralward. The ipsilateral foot, however, has stepped in the direction of the displacement.

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# THE ENCEPHALIC CONTROL OF TONE IN THE MUSCULATURE OF THE URINARY BLADDER.

BY ORTHELLO R. LANGWORTHY AND LAWRENCE C. KOLB.
*Sub-Department of Neurology, the Johns Hopkins University.*

## INTRODUCTION.

AFTER injuries to the spinal cord of man producing severe involvement of normal, voluntary micturition, the bladder, although it may contract automatically, never empties completely and there constantly remains residual urine. This was particularly well demonstrated by Head and Riddoch (1917) in their study of soldiers with complete transection of the thoracic portion of the spinal cord. Barrington (1925), on the basis of experiments with cats, localized in the cephalic portion of the hind-brain a centre controlling contraction of the bladder musculature. Following bilateral injury of small areas with the Horsley-Clarke stereotaxic apparatus, the contraction of the bladder musculature became faulty. These areas extended longitudinally from the level of the anterior end of the hind-brain in front to the middle of the motor nucleus of the fifth nerve below. The afferent impulses responsible for this motor control, according to Barrington, run principally with the parasympathetic fibres.

It is the current tendency in neurology to avoid the concept of isolated centres in the brain having specific functions, and to think of portions of the nervous system as large units correlating activity. On the basis of centres, it is difficult to understand an area controlling contraction of the bladder as removed from the cord and placed in the brain-stem. Taking a broader view-point, on the other hand, the brain-stem is known to have a powerful influence over the tone of the striated musculature of the body. It seems possible that a similar mechanism controls the tone of the smooth muscle in the bladder and that injury of this tonic mechanism or its pathway in the spinal cord may be responsible for the inability to empty the bladder completely. The present report deals with experiments which clarify this problem.

## METHODS.

Thirty-three adult female cats were used in the experiments. A fine glass cannula was inserted into the bladder through the urethra and the free end attached by a three-way tube to a water manometer with a three-millimetre bore. Through the three-way tube fluid could be introduced into the bladder from a burette graduated to $\frac{1}{10}$ c.c. Water, warmed to body temperature, was allowed to flow into the bladder slowly at the rate of about 1 c.c. a minute. Readings were taken after adding each 5 c.c.

The glass catheter was not tied into the bladder but was held in place by the tone of the urethra and the sphincters. When micturition began, the catheter became loose in the urethra and fluid escaped around the catheter. If the reflex of micturition was damaged so that retention resulted, fluid escaped when the pressure in the bladder rose to a level sufficient to force the sphincter. The insertion of the catheter without tying made it certain that the bladder never became overdistended. The apparatus recorded the phenomena of tone, and contraction of the bladder-wall, and relaxation of the sphincters was demonstrated only as a part of the reflex of micturition.

The type of anæsthesia to be used in the experiments was the subject of considerable study. Barrington felt that the bladder did not empty completely under ether anæsthesia. In our experiments with the cats quiet under light ether anæsthesia, the bladder usually emptied normally and completely. The pressure readings were often abnormally high after the administration of ether. The chief objection to this method was that the ether was discontinued after decerebration, inasmuch as the animals no longer felt pain, and it seemed hazardous to compare the results of reflex contractions under ether with those obtained after the anæsthesia was discontinued.

Several experiments were then performed using as an anæsthetic dial ciba in urethane which acted constantly throughout the whole period of the observations. This was kindly furnished by the Ciba Company. In order to avoid any possible local effect upon the bladder, it was not injected intraperitoneally but intramuscularly in amounts of ½ c.c. per kilogram. At least two hours were allowed to elapse between the administration of the drug and the beginning of the experiment. At the end of this time the preparation was extremely relaxed. A small amount of ether in addition was usually required at the beginning of the cerebral operation. Apart from this the anæsthesia was constant, so that the results of study of the bladder before and after decerebration are directly comparable.

The results of the experiments with these two anæsthetics agree in all important details. The bladder emptied reflexly upon a constantly smaller volume of fluid with dial than with ether. Certain facts were more clearly brought out with the use of ether. It is necessary to report in detail two typical experiments, one performed with the use of dial ciba and the other with ether.

## EXPERIMENTAL FINDINGS.

### (1) *Experiment utilizing Dial Ciba in Urethane as the Anæsthetic.*

#### (*a*) *Reflex micturition in the intact animal.*

After the cannula was inserted in the bladder of the cat, it was necessary to adjust the apparatus in such a way that the opening on the lateral side of the end of the catheter lay free in the bladder and accurate pressure readings were obtained. This was the most difficult part of the technical procedure. It is well known that the pressure in the bladder never falls to zero even when the viscus is entirely empty, and the pressure in the empty bladder in our experiments varied from 3 to 5 cm. of water. The initial reading was considered to be accurate when it lay within this range and when the column of fluid showed respiratory oscillations. This indicated that there was no block interfering with the readings.

Fluid was then slowly injected into the bladder, and the changes of pressure in the manometer were watched continuously and recorded after each 5 c.c. of fluid had entered. A graph showing the changes in pressure in the intact preparation is given (fig. 1 A) with the equal increments of volume plotted on the ordinates and the increments of pressure change on the abscissæ. In this case the initial pressure in the empty bladder was 4·5 cm. of water. With the addition of the first 5 c.c. of fluid the intravesical pressure rose to 13·2 cm. and remained below a pressure of 15 cm. of water until over 80 c.c. of fluid had been injected. The pressure then rose rapidly and complete evacuation of the bladder occurred when 94·2 c.c. had entered the viscus. As the volume of fluid was increased, waves representing weak contractions of the bladder musculature became superimposed upon the respiratory rises and caused variations, often of several centimetres, in the upper and lower readings. The lowest readings for a given period were always recorded for the sake of uniformity. When micturition occurred, the fluid expelled was collected, measured and compared with the amount introduced, giving a check of the ability of the bladder to expel the total contents.

This graph, showing variations of pressure in the cat's bladder with the addition of equal increments of volume, clearly illustrates the well-known fact that this hollow viscus can accommodate greatly increased amounts of fluid without altering materially the pressure within its walls.

Although the volume initiating reflex micturition varied for different preparations, it was remarkably constant for a given individual. To determine this readings were made upon a single cat on different days and with the use of each of the two anæsthetics, ether and dial ciba. The pressure readings were raised slightly by the administration of ether, and the bladder emptied with a somewhat smaller volume under dial. The volume of fluid necessary to induce reflex micturition was commonly around 60 c.c., although it could be lower and was commonly much higher.

The most convincing experimental results were obtained from individuals that showed reflex micturition only after more than 100 c.c. of fluid had entered the bladder. In these cases it was possible to show the change in volume initiating micturition after decerebration. The volume at which the bladder emptied in a given cat was always checked at least twice before the experiment was continued; it was necessary that the results should agree within 5 c.c. Many cats were rejected after initial readings on the normal bladder because the pressure readings were very high or because the viscus did not empty normally. These difficulties were ascribed largely to the anæsthetic, but there is undoubtedly great individual variation in bladder pressure and the volume required to produce reflex relaxation of the sphincters. The pressure readings were always somewhat high inasmuch as they were recorded simultaneously with the slow flow of fluid into the bladder under pressure.

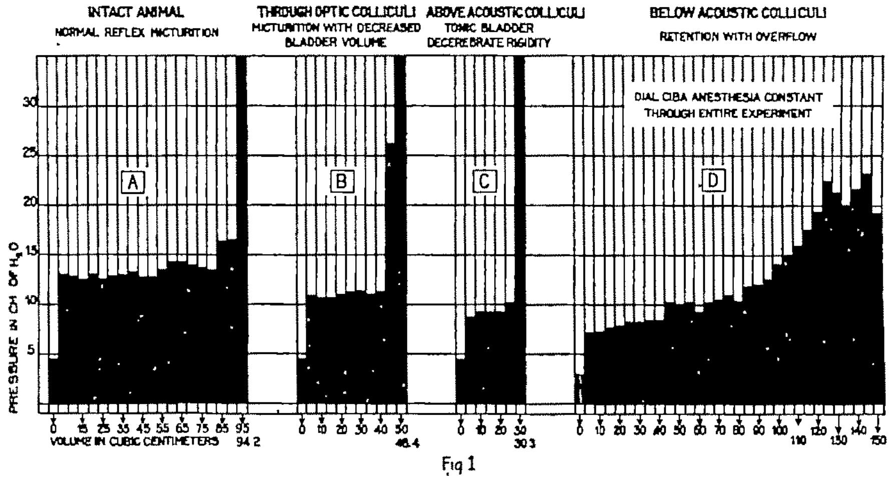

FIG. 1.—The addition of equal increments of fluid to the bladder volume is plotted on the ordinates, and the intravesical pressures in centimetres of water on the abscissæ. Dial ciba gave a constant anæsthetic for these results recorded from a study of a single preparation. Further description of the experiments is given in the text.

### (b) *The effect upon micturition of removal of the fore-brain to mid-thalamic level.*

The surface of the fore-brain was exposed bilaterally after the carotids had been tied, and a transverse cut was made through the nervous system above the mid-brain and through the mid-thalamic region. After this section there was no increased tonus in the extremities. When the reflex of micturition was studied, it was found that the bladder emptied on a volume 18 c.c. smaller than in the intact preparation. This result is not plotted in the graph. The significance of this variation, small in this particular experiment, will be discussed later in connection with other records made under ether anæsthesia.

### (c) *The effect upon micturition of transection through the optic colliculi.*

The second transverse section through the brain-stem passed through the cephalic portion of the optic colliculi. There was no appreciable increase in tone in the striated musculature of the extremities following this incision. The results in reference to the bladder are shown on fig. 1 B. The initial reading with the bladder empty was similar to that in the intact preparation, 4·5 cm. After the introduction of fluid the intra-vesical pressure remained lower than in the intact cat, and stayed constantly below 11·5 cm. of water instead of rising as high as 14·5 cm. of pressure. When the volume of fluid in the bladder had reached 40 c.c. the pressure rose very rapidly and forcefully and the bladder emptied on a volume of 48·4 c.c. of water. The most significant finding is the fact that the bladder, which in the intact animal had emptied only when it contained 94·2 c.c., now emptied on 48·4 c.c. of water. There were other changes. In the intact animal the musculature of the bladder showed rhythmical waves of contraction that increased in strength as the viscus became full; after removal of the fore-brain these waves of contraction were much less conspicuous. Moreover, the contraction of the musculature after the reflex of micturition was initiated was much more precipitous and stronger after transection of the brain-stem than it was before.

### (d) *The effect upon micturition of transection above the acoustic colliculi.*

After the preceding findings had been confirmed, the brain-stem was cut through at a slightly lower level, through the cephalic edge of the acoustic colliculi. Immediately after this cut, marked extensor tone could be demonstrated in the extremities. The volume of fluid in the bladder that was required for reflex micturition was then determined (fig. 1 C). The initial reading with the bladder empty was 4·5 cm., as in the intact animal. When further fluid was introduced the pressure remained below 10 cm. of water until the bladder emptied. This reading was not only lower than for the unoperated cat, but also lower than after transection through the optic colliculi. After 30 c.c. of water had been introduced, the bladder contracted forcefully and quickly and the viscus emptied completely. No significant rise in pressure occurred before the force of the contraction became great enough to empty the bladder.

After section through the cephalic edge of the acoustic colliculi, the bladder was found to empty reflexly and completely on less than a third of the amount of fluid required before the operation, and on considerably less than after transection through the upper edge of the optic colliculi. When the empty bladder was palpated through the abdominal wall it was felt to be very tightly contracted.

Data were obtained suggesting that the relaxation of the sphincters was more complete after transection of the brain-stem at this level than in the normal cat under the anæsthetic. In certain of the preparations before the operation, the relaxation of the sphincters with reflex micturition was very incomplete, and this was attributed to the anæsthetic. After decerebration with the same anæsthesia still operative, the relaxation of the sphincter was much more perfect.

### (e) *The effect upon micturition of transection of the brain-stem below the acoustic colliculi.*

The fourth section was made well below the acoustic colliculi; the increased tone in the extremities was not invariably lost and the cat breathed normally (fig. 1D). Now the picture of bladder activity was quite changed. The initial pressure with the bladder empty was 3 cm. of water, and the pressure rose after the introduction of fluid but always remained below 12 cm. of water until 90 c.c. had been introduced, the amount that stimulated micturition in the intact animal. The pressure readings were somewhat lower than in the record before operation. On the introduction of further fluid into the bladder, the pressure rose in graded increments and continued to rise until 125 c.c. had been introduced. Although waves of bladder contraction occurred, there was no well-sustained contraction that increased the pressure markedly and led to evacuation of the viscus. After 125 c.c. had been injected, the pressure was recorded as 23·5 cm. At this point there was a relaxation of the sphincter and a small amount of fluid escaped. During the injection of the next 10 c.c. of fluid the pressure fell, but rose again and each time it reached 23·5 cm., a small amount of fluid escaped. This experiment could be continued almost indefinitely without the development of any adequate reflex micturition. The bladder now showed retention with overflow, and the sustained contraction of the musculature required to empty the viscus was lost.

### (2) *Experiment utilizing Ether as the Anæsthetic.*

It is impossible at present to speak with certainty of the action of an anæsthetic upon the different portions of the nervous system, particularly its autonomic portion. The results obtained with the dial anæsthesia are reported to show that changes in the capacity of the bladder essential for reflex micturition are obtained after section of the nervous system when the anæsthesia remains constant throughout the experiment. The results when using ether as an anæsthetic bring out the part played by the cerebral motor cortex in the normal control of tone in the bladder musculature. Repetition of these results led to the conclusion that they were significant, the more so inasmuch as the ether anæsthesia was maintained at the same level after portions of the cortex were removed and indeed until the preparations were decerebrated. With dial care was taken to produce a deep anæsthesia which is reflected in the results of the experiments.

#### (*a*) *Reflex micturition in the intact animal.*

The results of a typical experiment using ether as the anæsthetic are shown in fig. 2A; the graphs are made after the same method used in the first table. The initial pressure reading from the intact preparation with the bladder empty was 5 cm. of water; with the introduction of the first 5 c.c. of fluid the pressure rose to 10·2 cm. and remained below 15 cm. until over 125 c.c. of water had been introduced into the bladder (fig. 2A). The pressure readings then rose fairly rapidly and after 155 c.c. had been introduced was over 30 cm. At this point the bladder emptied reflexly. The bladder of this cat had a large capacity.

#### (*b*) *The effect upon micturition of removal of the left motor cortex.*

After the normal capacity of the bladder had been ascertained, the left motor cortex was quickly exposed and cut away. The anæsthetic was con-

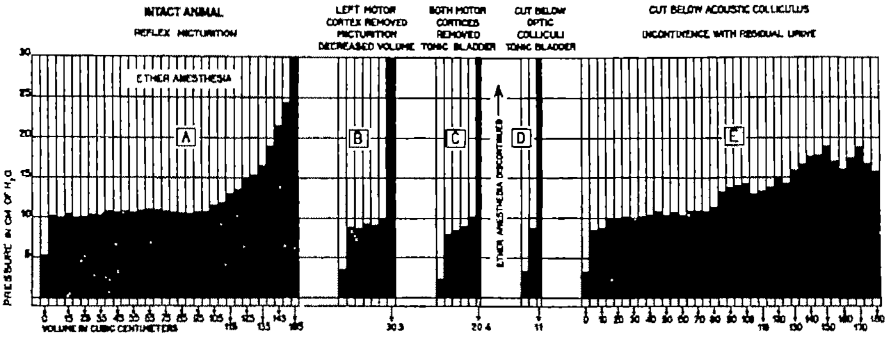

Fig 2

FIG. 2.—These results obtained from a single preparation under ether anæsthesia are plotted in the same manner as in fig. 1, and the results are further discussed in the text.

tinued and another determination of the capacity of the bladder was made (fig. 2B). The initial reading with the bladder empty was somewhat lower than before, 3·5 cm. as against 5 cm. The pressure rose with the introduction of water to 8·8 cm. and remained below 10 cm. of water until over 25 c.c. had been introduced into the viscus. The pressure then rose very rapidly to 33 cm. After 30·3 c.c. had entered the bladder, the sphincters relaxed, allowing the fluid to be expelled forcefully. Under the same degree of anæsthesia a bladder that in the intact animal showed an intravesical pressure of 30 cm. only after 155 c.c. of water had been introduced, now showed a pressure of 33 cm., as well as forceful contractions of the bladder musculature after 30·3 c.c. of water had entered the viscus.

### (c) *The effect upon micturition of removal of both motor cortices.*

With the depth of the anæsthesia held constant the right motor cortex was in like manner exposed and removed and another record of bladder activity was made (fig. 2C). The pressure after an initial reading of 2·4 remained below 10 cm. of water until 20 c.c. of fluid had entered the viscus; then the pressure rose so suddenly and rapidly that the bladder emptied completely around the catheter on a capacity of 20·4 c.c. and at a pressure of 24 cm. of water. Removal of the second motor cortex was followed by a second decrease in the size of the bladder so that it emptied on 20·4 c.c. as opposed to 30·3 c.c. after the cortex had been ablated on one side. Moreover, a bladder which held 155 c.c. in the intact preparation now contracted on 20·4 c.c. The rise of pressure with each of these sections became increasingly sudden and forceful, and the expulsion of fluid from the urethra more complete.

### (d) *The effect upon micturition of transection below the optic colliculi.*

The preparation was then decerebrated by transecting the brain-stem below the optic colliculi; following this operation the ether was discontinued. No time was allowed to elapse to enable the cat to recover from the anæsthetic, but as soon as the bleeding was controlled and respirations were normal, the investigation of the bladder was continued (fig. 2D). The animal showed increased extensor tone of the extremities. The initial pressure with the bladder empty was 3·2 cm. and rose after 5 c.c. of water had been introduced into the viscus to 8·2 cm. When 11 c.c. of water had entered the bladder the pressure rose quickly to 24 cm. and the bladder emptied completely around the catheter.

After transection below the optic colliculi, the bladder emptied reflexly on 11 c.c. of water instead of on 155 c.c. as in the intact animal and 20·4 c.c. after removal of both motor cortices. The expulsion of fluid was forceful and the pressure rose suddenly without initial oscillations.

### (e) *The effect upon micturition of transection below the acoustic colliculi.*

After the brain-stem was transected below the acoustic colliculi, the readings obtained from the bladder were greatly changed (fig. 2E). The initial pressure was 3·4 and remained below 15 cm. until over 125 c.c. of water had entered the bladder. Then the pressure readings rose very slowly; after 155 c.c. of fluid had entered the viscus and the pressure was 19·2 c.c. the sphincter relaxed and a small amount of water escaped from the urethra. The contraction of the muscle was very weak and after a small amount had escaped the sphincter tightened again and the pressure fell to 17 cm. The bladder now showed retention with overflow so that some fluid always escaped when the pressure rose to 19 cm., but the bladder never emptied. The transection of the brain-stem was below the centre controlling the tone and contraction of the bladder musculature.

## DISCUSSION.

These experiments confirm the findings of Barrington that the stimuli responsible for prolonged contraction of the musculature of the bladder essential for normal micturition are mediated from the region of the upper end of the hind-brain. Indeed, our work confirms exactly his findings concerning the level in the brain-stem of this control. It is not necessary, on the other hand, to postulate a unique and isolated centre for the control of the muscles of the bladder at this level, but rather to realize that tone in the bladder is determined by similar reflex pathways to those controlling tone in the striated muscles of the extremities. The technique used in the present experiments gives a more or less quantitative method for measurement of increased tone, whereas no good quantitative standard can be applied to the problem of tone in striated muscles.

The experiments with ether show convincingly that the tonic centre is normally controlled by both cerebral hemispheres. After the motor cortex has been removed on one side the bladder accommodates to a smaller volume of fluid before reflex micturition is initiated, and after both motor cortices have been removed the volume required to induce the reflex is further reduced. There are probably other controlling mechanisms in the fore-brain, either subcortical or in other portions of the cortex, for another reduction in volume is obtained after transections below the optic colliculi. The exact nature of this control has not been determined. If the transection of the brain-stem is then made below the acoustic colliculi, reflex micturition is abolished and the bladder shows retention with overflow. The tonic reflex responsible for contractions of the musculature adequate to empty the viscus have been abolished. We believe, therefore, that there is in the upper portion of the hind-brain a mechanism controlling tone in the smooth musculature of the bladder similar to the reflexes localized in the same region which control tone in the striated muscles of the extremities. This conclusion is unique in that a mechanism of this type has never been postulated for smooth muscle. The tonic reflex is responsible for prolonged and forceful contraction of the musculature necessary completely to expel the urine. The operation of this reflex is normally controlled and held in check by areas in the fore-brain and particularly from the cerebral motor cortex. When these inhibitory and governing mechanisms have been removed the tonic reflex overacts, as in the present experiments. After the connections of this tonic reflex arc with the spinal cord have been impaired in any way, incontinence with overflow is the immediate result and residual urine is always present even if automatic micturition becomes established.

That the tonic reflex for the bladder musculature is not the same as that controlling tone in the extremities is quite clear. Barrington could place lesions injuring bilateral areas in the medulla producing incontinence with overflow, but these preparations showed almost no disturbances of tone in the extremities. Using dial anæsthesia, the tonic reflex in the hind-brain could be released without producing decerebrate rigidity and, conversely, after a section below the acoustic colliculi the tonic bladder reflex was lost, but decerebrate rigidity still persisted.

These experimental findings serve to explain certain clinical symptoms. Patients with neurological lesions of the brain and spinal cord often complain that they have to micturate very frequently and that it is extremely difficult to hold back the urine after the first sensory impulses indicating distension of the bladder are received. The latter symptom is called imperative micturition. It indicates that the bladder can no longer be voluntarily relaxed to hold more fluid, and also that the contractions of the bladder musculature are immediately very forceful. It is probable in these cases that there has been a lesion of the inhibitory mechanism which governs the tonic mechanism in the hind-brain, and the condition is similar to that produced in the experiments by removal of one or both motor cortices or transection through the optic colliculi. The bladder empties upon small quantities of fluid and the contractions of the musculature are sudden and forceful.

Cases reported in the literature show that these abnormalities may be produced by bilateral lesions of the motor cortex. Thus Holmes and

Sargent (1915) reported cases of thrombosis of the superior longitudinal sinus. One patient explained that he was incontinent because he "could not hold his water for over five minutes." Imperative micturition also occurs when the lesion seems to be localized entirely in the spinal cord. This, of course, suggests that the inhibition of tonus is effected not at the level of the tonic reflex in the brain-stem, but through the motor cells of the spinal cord. Finally, it has already been explained that injury of the tonic reflex arc has a profound effect upon micturition in man.

The question may be raised as to the part played by contraction of the abdominal muscles in these experiments. Barrington rendered the abdominal wall functionless with curare and found that this had no effect upon his results. Although abdominal contraction may have a part in reinforcing micturition, it is by no means essential for the normal functioning of this reflex. The abdominal wall can be left open for only short periods of time without impairing the function of the musculature. However, we have opened the abdomen while the reflex was active without any impairment of its function.

One of the authors (Langworthy and Richter, 1930) has previously shown, using the galvanic skin response as a criterion of sweat-gland stimulation, that sweating, a function controlled by the sympathetic portion of the autonomic nervous system, was produced by stimulation of areas in the cerebral motor cortex and of all the well-known motor pathways extending from the brain to the spinal cord. The conclusion was reached that the activity of the preganglionic sympathetic cells is controlled by the same tracts that influence the somatic motor cells of the spinal cord. The present experiments suggest that tone in the bladder musculature is controlled by reflex pathways similar to those controlling tone in striated muscles. This discussion of the reflex of micturition probably has to do almost exclusively with the control of the parasympathetic reflex arc by the brain rather than the sympathetic portion of the autonomic nervous system as in the case of sweat-gland stimulation.

## SUMMARY.

The normal act of micturition is dependent upon a well-sustained contraction of the smooth musculature of the wall of the bladder. With lesions of the nervous system below the mid-brain affecting micturition, this contraction is faulty. The experiments were performed upon cats, using as anæsthetics dial ciba, which acts uniformly throughout the

experiment, or ether. After decerebration through the optic colliculi the bladder emptied completely on as little as one-fourteenth the volume of fluid required to produce reflex micturition in the intact, anæsthetized preparation. Under these conditions the pressure rose very rapidly and the contraction of the muscles was forceful. Transection of the brain-stem below the acoustic colliculi abolished this reflex and no contraction sufficient to empty the bladder occurred. The bladder then showed retention with overflow. The conclusion was reached that tone in the musculature of the bladder is controlled by similar mechanisms to those that control tone in the striated musculature. There is evidence that the control of this tonic mechanism is largely a function of the cerebral motor cortex and is effective at the level of the spinal cord. The tonic control is carried out from areas in the cephalic portion of the hind-brain. A study of bladder abnormalities in man serve to illustrate the experimental findings.

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# OBSERVATIONS ON THE PARALYSED BLADDER.

BY GORDON HOLMES.

THE observations recorded in this article were made in base hospitals in France during the War, mainly in the winters of 1915 and 1916. They have not been previously reported for various reasons, mainly because it was hoped to complete the investigation at the termination of the War by the examination of the later stages of paralysis of the bladder. This was undertaken in a few cases and the results obtained will be referred to. It was also realized that the methods employed were not adequate to solve many of the problems which arose, especially during the stages of recovery of tone in the musculature of the bladder. As more satisfactory methods of investigation have been devised by Denny-Brown and Graeme Robertson [1] these observations are now published as they throw some light on the condition of the bladder in the recent and acute phases of its paralysis as a result of spinal lesions, in which stage the opportunity of examining it is not so frequently met in civil practice.

*Material.*—With a few exceptions these investigations were made in men who had, as far as could be judged by clinical signs supplemented by radiological and surgical observations, complete transverse lesions of the spinal cord due to gunshot wounds. In a few cases with injuries of the sacral segments or of the cauda equina the lesions may have been incomplete. More than thirty cases in all were examined, and the injuries in these involved all regions of the cord from the highest cervical segments to the cauda equina.

In several cases the first examination was possible within two days of the infliction of the wound, but owing to the exigencies of hospital service during the War few could be kept under observation for long periods. Most men who received spinal injuries were evacuated to England within a week or ten days, but it was fortunately possible to retain a few cases for several weeks during periods in which there were few casualties. In some of these repeated examinations were made.

*Method of examination.*—The bladder was first emptied under strict aseptic precautions and a note was made of the amount of urine it contained. As it was found that the observations might be influenced by the degree of distention of the bladder before the examination, it was in most of the cases emptied half to one hour before measurements were made. A sterile saline solution was then introduced through the catheter at a slow and uniform rate and under pressure only just sufficient to allow it to enter freely. After each unit of volume, which was usually either two or four fluid ounces (60 or 120 c.c.), had entered the pressure within the bladder was recorded, and successive observations were made until the vesical pressure had reached a considerable height, or until the bladder contained an amount of fluid beyond which it was not considered advisable to go. The measurement of intravesical pressure was therefore intermittent, but the records were made at short intervals and any significant variations of pressure between the measurements were noted by an assistant.

In other experiments the changes of pressure within the bladder, when it contained a constant volume of fluid, were recorded. These observations were usually continued for several minutes, sometimes for as long as half an hour.

The apparatus used was necessarily simple. A large catheter was passed and held in position by an assistant. From it a rubber tube of equal calibre led to a large cylindrical reservoir containing sterile fluid which could be moved up and down along a scale marked in centimetres which indicated the height above the symphysis pubis, the point from which it was found most convenient to measure the head of the fluid. In order to obtain measurements of pressure the reservoir was raised or lowered till the level of fluid within it remained constant at a mark on its side. The height of this level was then read off on the scale and recorded.

A catheter and a tube of large bore were necessary to allow the fluid to escape freely from the bladder to the reservoir or to enter the bladder when the pressure within the latter varied rapidly, or when the reservoir was raised or lowered to determine the intravesical pressure. On the other hand, in order to introduce fluid slowly a tube of small lumen was essential. A by-pass was therefore provided in which a glass pipette of small calibre was inserted. During introduction of fluid into the bladder the main tube was compressed so that the fluid entered through the narrow by-pass only, but while the intravesical pressure was being recorded both the main tube and the bye-pass remained open.

After each examination the measurements were plotted on squared paper : the amount of fluid which the bladder contained on the abscissa, the corresponding pressure within the bladder on the ordinate. A curve of the volume-pressure relations was in this way obtained. The same scale has been used in all the tracings reproduced here.

This method of examination proved to be satisfactory in dealing with inert bladders in the early stages of paralysis, but in the normal, and in bladders regaining tone and reflex activity, rapid changes of pressure often occurred which could not be accurately measured. These can be demonstrated only by a method which records volume and pressure continuously, but such results as I obtained throw some light on the nature of early vesical paralysis and its recovery.

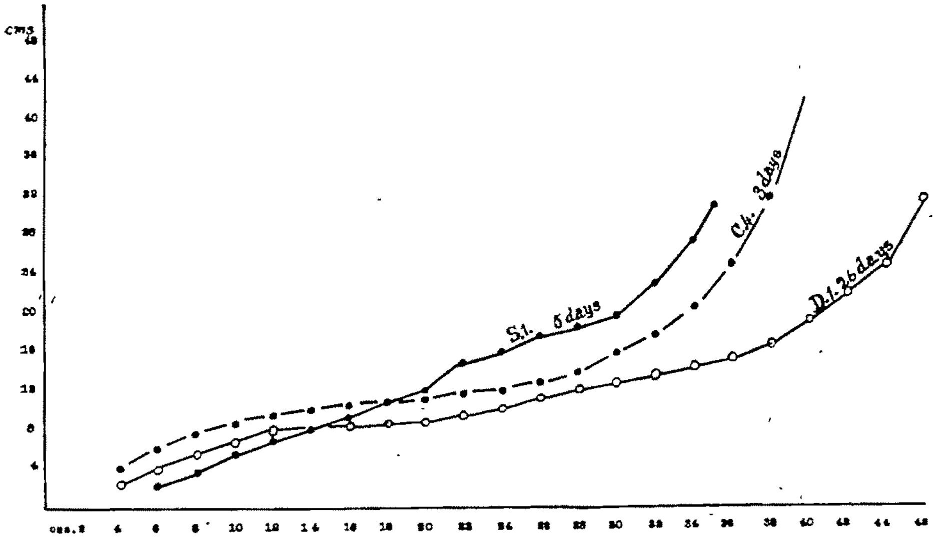

FIG. 1.—Tracings showing the volume-pressure relations obtained on filling slowly three different bladders. The lesions involved the first dorsal, fourth cervical and first sacral segments. The level of the lesion and the number of days after the infliction of the wound are shown on each tracing.

For the sake of simplicity the state of the bladder paralysed by a complete lesion of the cord will be described in the three successive phases through which it passes, but it must be understood that there is no rigid separation between these phases, which represent only stages in gradually progressing recovery of tone and activity.

*First phase.*—When the bladder of a man with a recent transverse lesion of the spinal cord was filled slowly, usually no pressure could be recorded, that is, the level at which the fluid in the reservoir remained stationary was below the level of the pubis as the patient lay on his back, until 4 to 8 oz. (120-240 cm.) of fluid was introduced. The amount of fluid that gave the first measurable pressure varied within narrow limits; as a rule it was greater when the bladder had been distended immediately before the examination, but in most of my cases it had been emptied half to one hour before the experiment.

As fluid was introduced the intravesical pressure rose slowly and gradually, never interrupted by an increase or fall unless some extraneous factor, as coughing, straining or pressure on the abdomen, came into action. The tracing obtained when the pressures were plotted was at first almost flat (fig. 1). No striking rise occurred until the pressure reached about 12 to 20 cm. of water, or till 20 to 30 oz. of fluid had entered the bladder. Then the curve rose more rapidly and when the pressure reached about 40 cm., no more fluid could be introduced under pressures which were considered safe; the bladder had apparently reached the limit of its distensibility. Even then no signs were observed of an attempt of the bladder to empty itself.

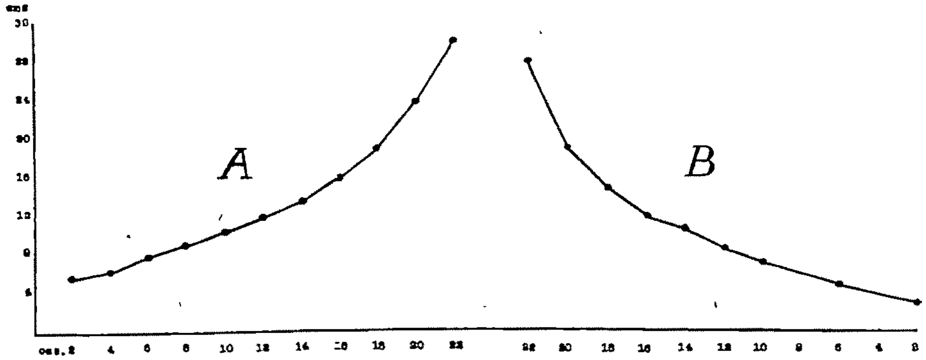

FIG. 2.—Lesion of fifth lumbar segment. Experiment 17 days after infliction of the wound. A, curve obtained on filling the bladder slowly; and B, that on emptying it at the same rate.

If the bladder was now emptied slowly and the pressure was recorded after each unit of volume was removed, the intravesical pressure fell gradually, and when the successive measurements of volume and pressure were plotted they reproduced a tracing practically the reverse of that obtained on slowly filling the bladder (fig. 2).

The recently paralysed bladder therefore presented the properties of elasticity only; that is, it resumed its original size or volume when the distending force which expanded it ceased to act, and in returning to its contracted volume the pressures which its walls exerted on its contents were equivalent to the force which expanded it to each similar degree.

When an amount of fluid sufficient to produce a measurable pressure in the bladder was kept constant and the pressure was recorded at short intervals no significant variations in the pressure, apart from those associated with respiration, were observed for several days or even three or four weeks after the infliction of the wound. When plotted the measurements of pressure formed practically horizontal lines (fig. 3). If the intravesical pressure were raised suddenly by pressure on the abdomen, coughing, or a deep breath, it fell at once again to its original level.

Within the first ten days or so after the onset of the paralysis the tracings obtained from these methods of investigation were practically identical in all cases examined. When the bladder had been greatly distended before the records were made, or if the state of the patient was unsatisfactory owing to sepsis of the wound or other complications, the curves were generally flatter, that is, intravesical pressure rose more slowly on the introduction of fluid, in other words the elasticity of the vesical musculature was diminished. On the other hand the occurrence of cystitis—and it was rarely possible to keep bladders which required frequent catheterization aseptic—had during this stage apparently little influence.

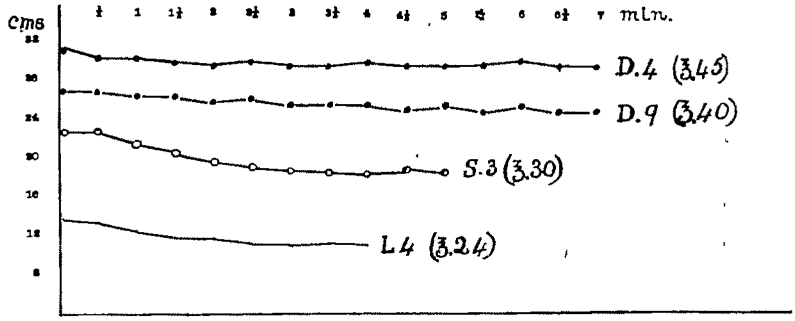

FIG. 3.—Tracings obtained in four cases by measuring the intravesical pressures at half-minute intervals when the volumes of fluid within the bladder were constant. The level of the lesion and the number of ounces of fluid in the bladder are shown to the right of each tracing.

From these series of observations it is obvious that the recently-paralysed bladder behaves as an inert elastic bag, and that it shows no tendency to adapt itself to its contents, or to react to the tension to which its walls are exposed.

The condition just described was always found when the bladder was paralysed by a transverse lesion at any level of the cord or of the cauda equina, in fact in the long series of patients examined no difference could be recognized, in the early stages of the injury at least, between cases in which the spinal origin of the hypogastric nerves had been destroyed or the cord had been injured above it, and those in which it escaped owing to the lesion lying below the 12th thoracic segment. Further, the effects on the bladder were very similar whether the lesion lay in the upper segments of the cord, or destroyed the sacral segments or their roots in the cauda equina. In both cases there was for a time apparently complete abolition of the nervous control of the bladder, which functioned only as an elastic bag.

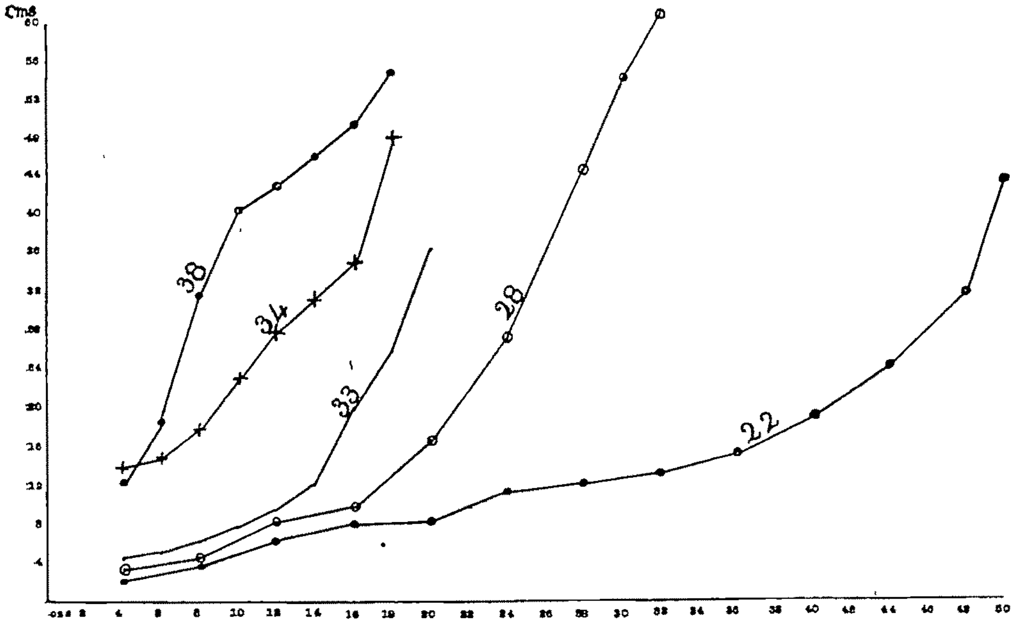

FIG. 4.—Five records showing the volume-pressure relations when the bladder was filled slowly on the 22nd, 28th, 33rd, 34th and 38th days after the onset of a complete transverse lesion of the first dorsal segment of the cord.

From these observations the conclusion seems inevitable that a transverse lesion of any segment of the cord produces a state of severe depression, or even abolition of function, i.e., spinal shock, in the vesical mechanisms in the isolated portion below the level of the injury.

*Second phase.*—When repeated examinations were made on successive days or at frequent intervals no change could be as a rule observed till two or three weeks after the onset of the paralysis.

As a rule the first change was an increasing resistance to the introduction of fluid; for instance, eight or even more ounces of fluid may have been hitherto necessary to produce a measurable pressure, but now a smaller amount might raise intravesical pressure to 10 or 12 cm. of water. The pressure curves also rose more rapidly (fig. 4). The amount of fluid which could be introduced into the bladder was also considerably less than hitherto. Frequently, too, the curve obtained from plotting successive measurements was less regular, particularly if any interruption or delay occurred during the experiment.

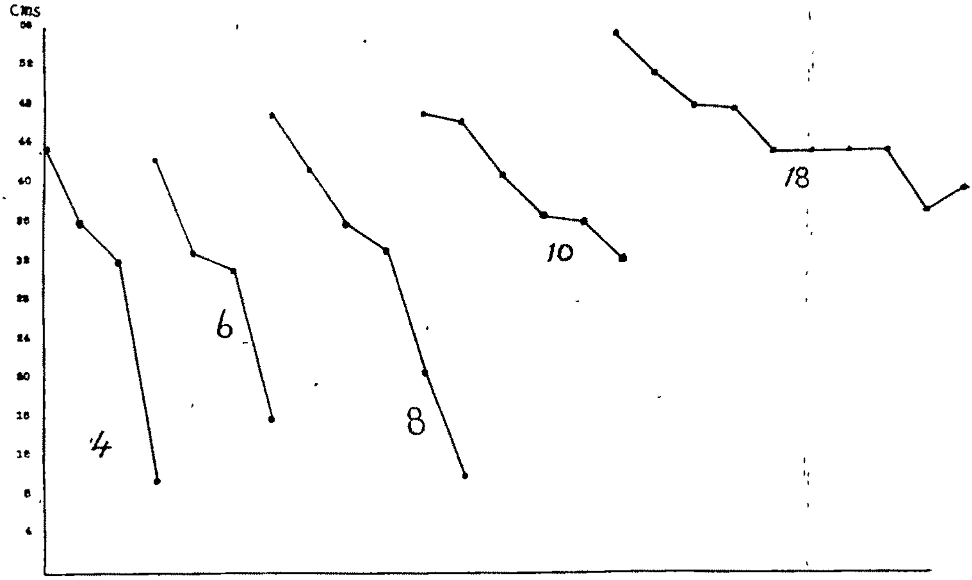

FIG. 5.—A series of tracings showing the fall of intravesical pressure after 4, 6, 8, 10 and 18 oz. of fluid had been in succession introduced into the bladder. In each instance the pressures were recorded at half-minute intervals.

If, when the intravesical pressure had been raised to a certain level the volume of fluid was kept constant, the pressure quickly fell, at first rather rapidly and then more slowly. This occurred no matter what the original pressure was, but the fall was usually greater and more rapid when the bladder contained a small amount of fluid only (fig. 5). When, however, a certain level of pressure was reached this level remained unchanged, apart from slight oscillations associated with respiration, for considerable periods, at least up to several minutes.

The pressure curves obtained during evacuation of the bladder were also now less regular; frequently the removal of a small amount of fluid led immediately to a considerable fall of pressure, which might rise again slightly before becoming steady.

At this stage the bladder had to some extent acquired again the property of adapting its size to its contents; its muscular wall had evidently regained some tone. The muscles of the paralysed limbs were at this time still quite toneless, and the reflexes of the legs were usually absent.

It is worthy of note that these manifestations of tone appeared even when the sacral segments of the cord or the cauda equina were injured, but within the first few weeks of the infliction of the wound it was more difficult to determine the severity of the lesion when the roots were involved than when the cord was wounded. In the case from which the readings in fig. 6 were obtained the clinical symptoms indicated a severe lesion of all the sacral roots; there was evidently a considerable return of tone on the eighteenth day as compared with the fourth day after infliction of the wound. This recovery of tone can be seen in another case (fig. 7) in which the cauda equina was injured by a large piece of metal which entered the vertebral canal through the fourth lumbar lamina and produced complete loss of sensation on all the sacral root areas on both sides and on the fifth lumbar area also on the left. There was no recovery of sensation during the three weeks the patient remained under observation.

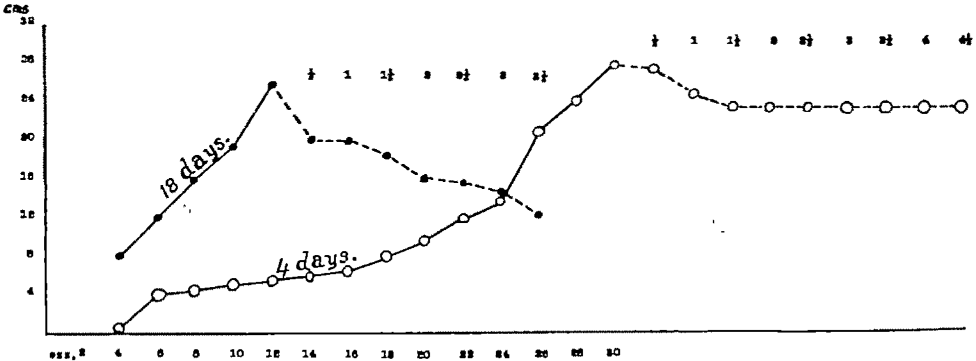

FIG. 6.—Two tracings showing the filling curves and the changes in pressure to constant volumes of fluid, 4 and 18 days after severe injury to all the sacral roots in the cauda equina. Time is recorded above in half minutes.

*Third phase.*—The stage of simple tonicity of the bladder was generally of short duration and passed gradually into the third phase, the distinguishing feature of which was the occurrence of sudden contractions of the bladder producing increases of intravesical pressure, or even the escape of fluid or extrusion of the catheter.

The tone of the musculature was evidently still increasing, for the curves obtained by plotting the initial pressures against the volumes which the bladder contained were steeper than hitherto (fig. 4, thirty-four and thirty-eight days). Less fluid could be introduced under moderate pressure, and the bladder adjusted itself more readily to its content; consequently the intravesical pressure no longer bore any definite relation to the volume of fluid within the bladder.

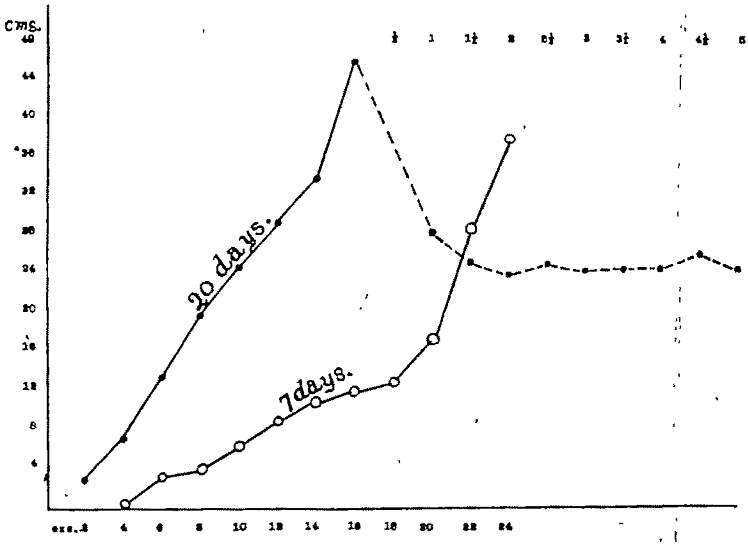

FIG. 7.—Two filling curves obtained 7 and 20 days after the onset of a lesion of the cauda equina. On the 20th day, after 16 oz. of fluid had been introduced, this volume was kept constant and the intravesical pressure was recorded at half-minute intervals for five minutes.

When the volume of fluid was kept constant the pressure frequently varied, rising and falling within wide ranges. These oscillations of pressure occurred irregularly and often were apparently spontaneous, at least they could not be associated with any other phenomenon.

They were generally not recognizable till the third or fourth week after the onset of the paralysis, and in some cases they appeared before the muscles of the legs had recovered tone or reflex spasms had developed. Two tracings representing these oscillations of pressure in one patient are reproduced. In one experiment (fig. 8), 10 oz. of fluid raised the intravesical pressure to 44 cm. of water, but it soon began to fall, at first abruptly, then more slowly, so that after two minutes it was little more than half its original height. It remained at this level or with slight variations for about four minutes, when it rose so suddenly that some of the fluid was evacuated into the reservoir with such force as to indicate a powerful and abrupt contraction of the bladder. The pressure then subsided quickly to 28 cm., and later fell more gradually, so that nine minutes after the experiment began it was only 14 cm. Later, without obvious cause, another small rise occurred. Sometimes several such contractions of the bladder could be observed in succession at fairly regular intervals (fig. 9), especially in the early stages of this phase.

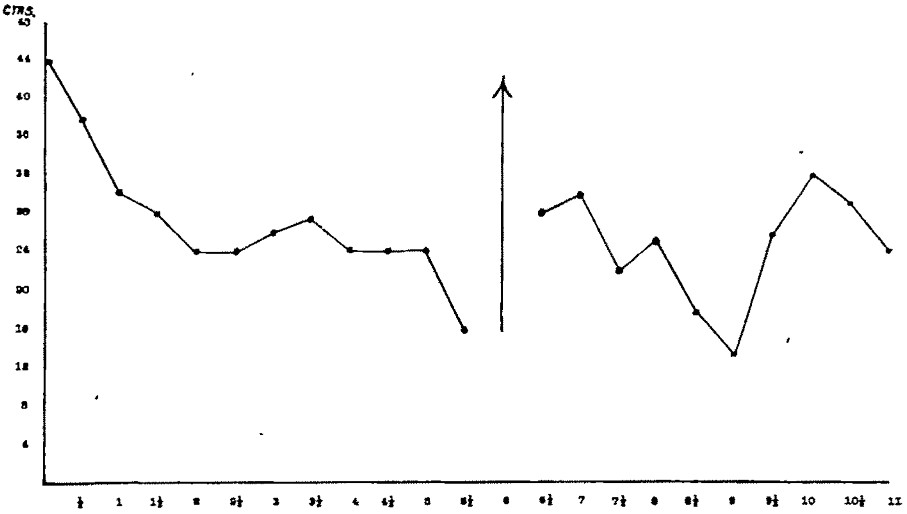

FIG. 8.—To show the variations in intravesical pressure when the bladder contained 10 oz. of fluid. The measurements of pressure were recorded at half-minute intervals. The arrow indicates a sudden rise of pressure and escape of some fluid into the reservoir. A transverse lesion of 1st dorsal segment 34 days after onset.

The amount of fluid which the bladder contained had little influence on these contractions, but they were observed only when the intravesical pressure was at least moderately high. The experiments recorded in figs. 8 and 9 were made on successive days; on the thirty-fourth day 10 oz. of fluid raised the pressure to 44 cm., but on the following day 20 oz. produced a pressure of only 38 cm.

These oscillations of pressure were observed in bladders paralysed by lesions at different levels of the spinal cord, but they seemed to develop later and to be less pronounced when the lower segments were injured. I have no definite record of them occurring after complete division of the cauda equina, as when these investigations were made there was no opportunity to keep patients with such lesions sufficiently long under observation, but slight variations in pressure were seen in cases in which the sacral roots had been injured three or four weeks previously.

Though these sudden contractions of the bladder often occurred apart from any other disturbances, they were sometimes associated with reflex spasms of the legs and abdominal muscles if the spinal lesion is sufficiently high for these to develop. They could also be excited by suddenly raising the pressure within the bladder, or by making the patient cough or strain. A rapid increase of tension on the walls of the bladder was evidently an effective stimulus.

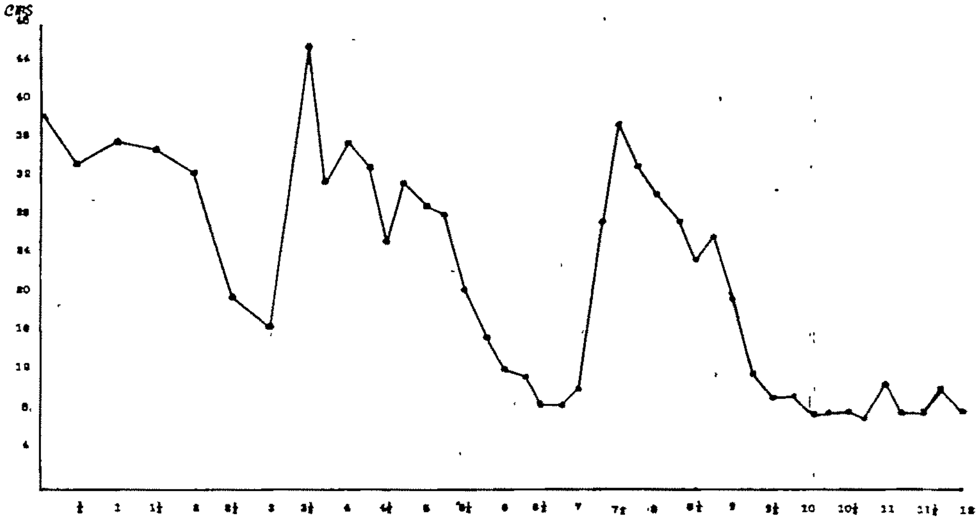

FIG. 9.—As in fig. 8 the bladder contained 20 oz. of fluid. Transverse lesion of 1st dorsal segment 35 days after infliction of the injury.

It sometimes happened that during a contraction of the bladder the catheter was extruded and fluid escaped, often leading to complete evacuation. This frequently followed a series of contractions which culminated in one which raised the intravesical pressure to an exceptionally high level. It might be associated with reflex spasms of the legs and abdominal muscles excited by a stimulus to the lower limbs or to the perineal region, but it was then repeatedly observed that the contraction of the bladder and its evacuation followed the spasms of the legs and abdomen by a definite interval of time, sometimes by several seconds.

The following conclusions can be drawn from my observations. Immediately after a complete transverse lesion of the spinal cord at any level, or of the cauda equina, the bladder acts merely as an elastic reservoir and shows no signs of nervous activity. After a variable interval evidences of returning and gradually increasing tone of the musculature of the bladder-wall appear. Shortly after this the bladder becomes a reflexly active organ, at least when the lesion lies above the sacral segments of the cord.

No suitable apparatus was available with which to investigate the state of the sphincters, and such observations as were made add little to the general knowledge of their behaviour in acute spinal lesions. Within the first week or so of the onset of the paralysis a definite resistance was generally felt in passing the catheter through the sphincters, and there was usually no difficulty in keeping it in position or tendency for leaking to occur round it. It may be therefore assumed that at this stage, when the bladder was toneless, the sphincters preserve some tone. This corresponds with the fact that overflow incontinence generally develops later, and that it may be impossible to express urine during the first one or two weeks by pressing upon or massaging the bladder.

A little later, usually during the second or third week, it was often more difficult to keep the catheter in position and fluid escaped readily around it, indicating that the tone of the sphincter had become less. At this stage overflow incontinence was not uncommon. Later, when the bladder has regained tone, more resistance was experienced to the introduction of the catheter, and the sudden extrusion of the catheter and the evacuation of the bladder which often occurred, indicated that not only was the sphincter in a state of tonic contraction, but that it was also capable of reflex activity.

Attention may be drawn here to interesting observations published by Fullerton [2] on the state of the ureters and of the uretero-vesical sphincters early after the onset of complete transverse lesions of the cord, many of which observations were made on the same patients as my own experiments.

The ureteric orifices were inspected through a cystoscope after an intramuscular injection of indigo-carmine had been administered in order to observe more easily the urine issuing from them. Several cases with complete lesions of the cervical and dorsal segments were examined, and his conclusions were:—

(1) Peristalsis of the ureters continues, as evidenced by the rhythmical discharge of urine from them.

(2) Normal movements of the lips of the ureteric orifice take place, as shown by its visible systole and diastole.

(3) The tone of the uretero-vesical sphincter is maintained and the valve is competent.

It is obvious from these observations that the ureters and their sphincters behave differently to the bladder and its sphincters after the spinal cord has been damaged by a severe transverse lesion.

It is not intended to refer to the extensive literature on paralysis of the bladder, but the work of Head and Riddoch [3], published in 1917, deserves comment, more especially as some of the conclusions to which they came are not supported by my observations. This may be partly due to differences in the methods employed, for they measured only the amounts of fluid introduced into the bladder, not the intravesical pressure, and, as has been shown, there may be no close relation between them. My observations suggest that the intravesical pressure is a much more important factor in determining the activity of the bladder than the amount of fluid it contains.

Head and Riddoch described automatic emptying of the bladder as part of a "mass reflex" which could be evoked by stimulation of the legs and other parts below the level of the spinal lesion. They attributed this to "a vast outburst of motor energy . . . overflowing into visceral channels," or a wide irradiation of the reflexes due to loss of "local signature" in the cord.

Involuntary micturition was repeatedly observed and studied in the course of my experiments, and it certainly often followed spasms of the lower limbs which were either purposely excited or apparently spontaneous. My observations indicate, however, that the contraction of the bladder which occurred in these circumstances was not an immediate result of stimulation of the legs, but that it was due to the associated spasm of the abdominal wall which, by raising the intra-abdominal pressure, increased suddenly the tension on the vesical musculature.

The following facts point to this explanation: Evacuation of the bladder frequently followed a series of apparently spontaneous oscillations of intravesical pressure, which were usually not associated with spasms or other reflex movements of the lower limbs. It could also be produced by suddenly augmenting the pressure in the bladder by raising the reservoir of fluid in connection with the catheter, or by increasing suddenly the intra-abdominal pressure by coughing, deep breathing or a sudden compression of the abdomen.

When the lesion of the cord was sufficiently high flexor spasms of the legs were usually followed by, or associated with, vigorous contraction of the abdominal wall which must raise intra-abdominal pressure. If the intravesical pressure was observed under these circumstances it was seen that the contraction of the bladder did not occur simultaneously with the spasm of the abdominal wall, but after an interval, suggesting there was not an immediate overflow of innervation into the visceral centres in the cord. A short series of oscillations of pressure often preceded the more vigorous contraction which expelled the contents of the bladder.

The importance of abdominal spasm in exciting reflex micturition is well illustrated by a case described by Head and Riddoch [Case 8], in which scratching the right sole excited flexor spasms of the right leg, "a strong contraction . . . in the right half of the abdomen" and evacuation of the bladder; while on similar scratching of the left sole "the reflex movement was violent, but there was little or no movement of the abdomen" and "the energy evoked could not materially affect the activity of the bladder."

Further, though flexor spasms of the legs often extend to the abdominal wall, reflex extensor movements excited by peripheral stimuli usually do not do so, and they are less likely to be followed by reflex incontinence. Head and Riddoch in fact assert that "so long as extension can be obtained as a primary reaction energy does not overflow into visceral channels."

Finally, where the lesion lay so low in the cord that the reflexes excited in the lower limbs did not spread to the abdominal muscles, stimulation of the soles had no influence on the bladder.

From these facts it must be concluded that the evacuation of the bladder which follows stimulation of the lower limbs is not part of a "mass reflex," and that impulses arising from the periphery of the limbs do not spread to the spinal vesical mechanisms. The micturition which occurs under these circumstances is a result of the associated spasm of the abdominal muscles producing a sudden increase of intra-abdominal pressure; this augments the tension within the bladder and therefore excites it to contraction.

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# THE STATE OF THE BLADDER AND ITS SPHINCTERS IN COMPLETE TRANSVERSE LESIONS OF THE SPINAL CORD AND CAUDA EQUINA.

BY D. DENNY-BROWN AND E. GRAEME ROBERTSON.

(*From the National Hospital for Diseases of the Nervous System, Queen Square, London.*)

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## I.—INTRODUCTION.

DISTURBANCES of micturition as a consequence of partial lesions of the spinal cord are frequently difficult to interpret in terms of current views of vesical function. We have elaborated a method of investigation of such disturbances, and our findings in a number of cases convinced us of the necessity of the examination of normal micturition and analysis of the disturbances following complete lesions of the spinal cord and cauda equina, before the analysis of partial lesions can be attempted. We have already described normal micturition [15], and here bring forward the outcome of our investigations of complete lesions.

A most complete and accurate review by Fearnsides [17] covers most of the literature of the subject up to that time. Since the subject is complicated, however, we shall first describe such work as appears to have direct bearing on our own problems.

The involuntary musculature of the vesical wall (detrusor) and of the internal sphincter receives innervation from two regions of the spinal cord: One innervation is derived from the lumbar sympathetic chain via the inferior mesenteric ganglion and hypogastric plexus (hypogastric nerves), the other from the sacral plexus by the pelvic nerves (sacral nerves or nervi erigentes). These two outflows intermingle in the vesical plexus of outlying ganglion cells and fibres which directly innervates the bladder and sphincter. The voluntary musculature surrounding the deep urethra (external sphincter) and the associated voluntary musculature of the perineum is innervated by the pudic (pudendal) nerves. Both the pelvic and the pudic nerves are derived from the second, third, and fourth sacral roots (Waldeyer [54], Head [26], Harman [25]), and corresponding segments of the spinal cord, while the hypogastric plexus through the sympathetic chain is derived from the eleventh and twelfth dorsal and first lumbar roots (Head [26], and Harman [24]), and corresponding segments of the cord. All three sources of innervation convey afferent fibres, amounting in animals to one-third the total number of fibres in the pelvic nerve, but only one-tenth in the hypogastric nerve [33, 34, 35].

Stimulation of the peripheral segment of the cut pelvic nerves in animals induces powerful contraction of the detrusor musculature with relaxation of the internal sphincter (Gianuzzi [20], Von Zeissl [59, 60], Elliott [16], and others). Stimulation of the hypogastric nerves causes contraction of the internal sphincter in all animals, including man (Learmonth [38]), accompanied by a degree of inhibition of the detrusor which varies with the species of animal employed (Elliott [16]). Stimulation of the pudic nerve contracts the external sphincter. Section of both pudic nerves in an otherwise intact animal leads to occasional slight incontinence [3]. Section of both pelvic nerves occasions a profound depression of micturition with an atonic distended bladder (Lannegrace [37], Elliott [16], Barrington [3]). This condition changes after a few days to intermittent micturition in small jets, each expressed only by powerful effort in the cat, and is further changed to intermittent spontaneous dribbling from a small bladder by later section of the pudic nerves (Barrington [3]). Subsequent section of both hypogastric nerves apparently has no effect on any of these disturbances

(Barrington). Section of the hypogastric nerves results in either no change [40], or but a slight frequency of micturition [3], and urine is still held at the internal sphincter (Barrington [3]). Section of all three sources of nerve supply is followed, after a short period of retention, by periodic discharge or "automatic micturition" (Dennig [14], Elliott [16], Wlasow [58]). The integrity of the pelvic nerves, therefore, appears of paramount importance to the adequate performance of normal, "voluntary" micturition.

Complete destruction of the lumbo-sacral segments of the spinal cord causes atony of the bladder with a resistant sphincter and resultant retention of urine. This state passes in the course of a few days to intermittent discharge from a small bladder (Goltz and Ewald [22] and Müller [41]). The effect is the same as that of combined section of both pudic and pelvic nerves. Goltz and Ewald observed that the subsequent state is one of intermittent automatic micturition. The detrusor musculature becomes remarkably hypertrophied.

Complete transverse section of the spinal cord above the lumbar segments in the dog and other animals is also succeeded, after a period of depression of function, by the development of a process of "automatic micturition." Large quantities of urine are periodically voided, each in a steady stream which almost or completely empties the bladder (Goltz [21], Sherrington [49]). Light momentary intermittent abdominal pressure, or stimulation of the perineum, facilitates its occurrence, strong stimulation of the reflexly active limbs causes it to cease (Sherrington [48, 49]). This automatic act in the spinal animal is accompanied by defæcation and a motor reflex in the tail [48]. Differences in level of section of the cord make no change in the development of the process. Barrington [3] states that in cats the external sphincter (compressor urethræ) is highly tonic in the period of depression and becomes less tonic as automatic micturition is developed, but in another place [7] states that this part of the urethra in the cat still retains resistance to outflow even when the pudic nerves are severed. In the spinal animal stimulation of the whole sciatic nerve is stated to cause micturition [51, 16], with relaxation of the internal sphincter [16], but this effect was not obtained from the internal pudic or small sciatic nerves [16]. Distension of the bladder has long been recognized as an adequate stimulus for reflex micturition [21, 23].

The effect of various partial sections of the spinal cord in animals indicates that the pathways controlling micturition travel in the most dorsal part of the lateral column, in the region of the pyramidal tract, and that one such pathway on either side is alone sufficient to maintain control if the other be impaired [40, 9]. There is evidently much decussation of the fibres concerned in the lumbar and sacral segments [9, 51].

Barrington [3] describes five separate reflexes arising from the bladder and urethra and activating micturition. The first reflex is contraction of the bladder in response to increasing volume of contents, and the second secures strong contraction of the bladder when fluid forces the sphincter and runs through the urethra. Distension of the proximal urethra not sufficient to force the external sphincter causes a slight rise of vesical pressure and this forms the third reflex, while the fourth reflex is an active relaxation of the urethra when it is passively distended. By "urethra" he refers to the most proximal segment, which in the cat is surrounded by smooth muscle continuous with the neck of the bladder. There seems little objection to identifying the smooth muscle with what is ordinarily meant by internal sphincter. The fifth reflex secures relaxation of the external sphincter whenever the bladder makes response to distension. Barrington has shown that the first reflex has both afferent and efferent pathways in the pelvic nerves, for the second the pudic nerve is afferent and the pelvic efferent, for the third both pathways are in the hypogastric nerves, and for the fourth both pathways are in the pudic nerves. The fifth reflex has its afferent pathway in the pelvic nerve and efferent in the pudic nerve.

Barrington further states that the first reflex, the response of the bladder to distension, arises in the central nervous system at about the level of the plane through the posterior parts of the inferior colliculi dorsally and the middle of the pons ventrally [5, 4] and that the second reflex also completes its reflex arc in the brain-stem. The other three reflexes still occur in the spinal animal.

On the basis of the series of reflexes thus described the automatic micturition of the spinal animal remains unexplained except as a consequence of a leak past the internal sphincter. In a later paper, Barrington [8] describes a sixth reflex which is a relaxation of the plain muscle of the urethra by distension of the bladder after spinal transection. Thus some overflow might be expected from extreme distension, and this indeed is the condition of the "chronic" spinal cat as described by Barrington. It is, however, apparent to those who have worked with the reflexly-active spinal dog that forceful and apparently complete micturition can occur, and one must conclude that in this animal, which can be kept in the chronic spinal state with much greater ease and with much fuller recovery of limb reflexes than the cat, vesical reflexes other than the third, fourth, fifth and sixth reflexes of Barrington are active.

In the decerebrate cat, Barrington [5] describes micturition as a forceful stream, each micturition terminating in a series of minor jets accompanied by perineal contractions. Stimulation of the perineum can provoke micturition. There is frequently some residual urine, and Barrington argues that decerebrate micturition is "inco-ordinate" on account of this lack of completion.

The effect of complete destructive lesions of the sacral segments of the spinal cord in man, as in animals, has long been recognized to be followed, after a period of retention, by automatic micturition (L. R. Müller [41], Bálint and Benedikt [2], Oppenheim [42], Schwarz [46], Adler [1]), which takes the form of "periodic incontinence" or "active incontinence ("active paralytic overflow" [12]). The bladder may become small and hypertrophied as in animals (Lhermitte [39]). After verified lesions of the conus there has been described a lack of natural desire for micturition, though involuntary micturition is often preceded for a few minutes by a feeling of tightening in the lower abdomen, and undue distension may cause pain [32, 41, 2]. It has been claimed that sense of distension of the bladder may remain unaffected (Riddoch [44]). No other function attributable to the intact hypogastric innervation of the bladder (D. 11—L. 2) has been demonstrated in these cases. Passage of urine can be secured by passive pressure or by a voluntary contraction of the abdomen by the patient [18], but apart from this there exists true involuntary automatic micturition which most usually takes the form of frequent discharge of small quantities of urine, but may develop into complete evacuation of a larger volume in a powerful steady stream five to six times a day [41, 2, 18]. A severe toxæmia is accompanied by gradual loss of automatic vesical function and redevelopment of complete retention [2]. This type of automatic micturition may be established following widespread destruction of spinal cord [11].

The occurrence of automatic micturition in man as a consequence of a complete transverse lesion of the spinal cord above the level of the sacral segments has also long been recognized [18]. When the condition is fully developed, large quantities of urine may be expelled by each micturition and the bladder completely emptied. The vesical pressure rises steeply during filling [1, 46]. When the bladder is filled a reaction occurs, as in the automatic bladder after conus lesions, but is here much more powerful, so that the vesical pressure often rises well over 100 cm. water pressure even with small volume of vesical contents (Frankl-

Hockwart and Zuckerkandl [18], Schwarz [46] and Adler [1]). This type of micturition has been distinguished as the "hypertonic bladder," as opposed to the relatively "atonic bladder" of automatic micturition following cauda equina lesions [18]. Though the stream is more powerful when micturition occurs from the hypertonic bladder, it is maintained that the discharge of urine is not easily obtained by steady pressure upon the abdomen, and a regular massage is necessary [18]. The sphincter offers resistance to catheterization, and estimation of the pressure necessary to overcome it shows usually that this is raised above the normal [39]. Percussion of the lower abdomen, on the contrary, facilitates micturition [18], as does also "reflex" stimulation [18, 42], such as passage of a catheter through the urethral meatus or stimulation of the glans penis. The height of segmental level of spinal transection has no relationship to the type of vesical disturbance resulting [55]. It has been maintained that the initial period of retention of urine in man is associated with powerful contraction of the internal sphincter (Rehfisch [43]). Though vesical contraction in response to filling is then usually absent, the detrusor is able to expel its contents through a catheter late in this period [27].

The "hypertonic" automatic bladder is often more difficult to catheterize than the less tonic automatic bladder following conus lesions, and it has been held by Müller [41] that the former type of automatic micturition differs from that following conus lesions only in the presence of effects attributable to the undue tonicity of the sphincters. The reaction of the "hypertonic" bladder to filling has been shown by Holmes [29] to be due to long slow fluctuations of vesical pressure which are more readily elicited as the phase of retention passes. Head and Riddoch [27], as a result of observations on the recovering reflexes in cases of complete transverse lesions of the spinal cord in man, found that at a certain stage of recovery elicitation of the flexion reflex facilitates discharge of the vesical contents through a catheter. This phenomenon occurred when the bladder contained less fluid than was required to stimulate automatic discharge, and was explained on a hypothesis of a spread of reflex effect in the recovering isolated segments of the cord, with resulting massive reflex discharge of flexion, micturition and sweating in response to any cutaneous stimulus, "the mass reflex." The teleological basis of this "primitive reaction" has been strongly criticized (Walshe [56, 57]). Schwarz [46] in his series of cases failed to elicit micturition by cutaneous stimulation.

The spontaneous fluctuations of vesical pressure originally observed in the human bladder by Mosso and Pellacani [40], and in animal bladders by many investigators (Sherrington [47], Stewart [53], Elliott [16]), have been occasionally observed in manometric observation in work on the human bladder, and Holmes [29] has traced the emergence of rhythmical contraction during recovery from the depression of spinal shock. There has been, as far as we can ascertain, no analysis of the part played by rhythmical vesical contraction in vesical function.

Though in the course of our investigation we have subjected some twenty-nine patients to detailed investigation we have found only three lesions of the cauda equina and three spinal transections, with sufficiently discrete and complete lesions, of sufficiently chronic nature to demonstrate their constancy, and of sufficient duration of recovery from the effects of shock to give evidence of the fundamental principles underlying the disorders.

## II.—METHOD.

The primary object of the present investigations has been to seek information as to the exact form of vesical activity and correlated sphincteric disturbance in spinal lesions and the relationship of these to the phenomena readily observed clinically. For this purpose records of the vesical and urethral pressures during micturition were chosen as indicative of the phases of vesical activity.

Records of vesical pressure have been made by a technique which has been described in detail in our earlier communication [15] of control experiments in normal bladders. The method consists of the introduction of two catheters so that a narrow catheter lies within the lumen of an ordinary rubber catheter. Through one the bladder is filled with sterile warm saline, and the vesical pressure is recorded by mirror manometers connected to each catheter. Subsequent withdrawal of the larger catheter into the urethra allows the registration of the discharge through the sphincter to be made by the manometer of this catheter while vesical pressure is concurrently recorded by the other. It was found necessary to record intra-rectal pressure and movements of the abdominal wall and the perineum concurrently in order to estimate the effect of extravesical changes. The records were made on a slowly moving strip of bromide paper by the beams of light reflected by the manometers. Time is recorded by a rotary time marker showing one-fifth second intervals. To avoid overlapping of records the manometers recording rectal and abdominal pressures are arranged to show a downward deflection for increase of pressure on the balloons, the other tracings make upward movement for increase of pressure.

In recording discharge of a sphincter the urethral catheter connection is allowed to leak through a narrowed side opening. The column of fluid in the catheter records the impact of discharge of even one drop of urine with very brief latency (some 0·01 second).

Our own method, on account of the numerous controls necessary and the bulk of apparatus required for long running records, is not readily applicable at the bedside. In its essential principle of measurement of the vesical pressure, however, we believe that all the data bearing on the vesical pressure may be readily observed by more portable apparatus such as was used by Gordon Holmes, or by the portable cystometer introduced by Rose [45, 45A], provided that the rate of filling with such apparatus is slow, and adequate time given for adaptation of pressure to volume. A number of the smaller fluctuations will be observed only with difficulty in a mercury manometer.

We have not had access to patients in the early stages of complete lesions. The work of Gordon Holmes, published in the preceding paper in this Journal [29], carried out also by measurement of vesical pressure, surveys disturbances at this period, and provides us with the necessary perspective.

## III.—The Reaction to Distension.

Allowing the bladder to fill slowly from a reservoir brings about a gradual rise in the vesical pressure which reflects the resistance offered to the entering fluid by the musculature of the vesical wall. In order to estimate the power of adaptation of the bladder to the volume of its contents our usual procedure was to close the inflow after the introduction of each 100 c.c. of fluid and for an interval to record the behaviour of the bladder at constant volume before allowing the next 100 c.c. to enter. The fluid was introduced slowly through a narrowed orifice under a steady pressure of 50 cm. reservoir level height. The rate of filling, unless expressly stated otherwise, is slow (see figs. 8 to 13) but is not constant owing to the variable resistance to inflow provided by slight differences in the apertures of different catheters and the pressure of vesical contents. The narrow catheter materially lessens the aperture of the larger catheter through which it passes. The clinical state of the patients is described in the Appendix.

### (1) *The Effect of Lesions of the Cauda Equina.*

In comparison with the bladder of a normal subject the vesical pressure in Case 1 mounted rapidly as volume increased, so that at a volume of 200 c.c. it had reached 70 cm. of water (fig. 1). The rise of pressure was at first regular (fig. 8 A) but as the volume was maintained at 100 c.c. a series of fluctuations of pressure made their appearance in groups of two and three (fig. 8 B), associated with discomfort. These reappeared after increasing the volume to 150 c.c. (fig. 8 D), and again at 200 c.c. (fig. 9 A). It will be observed that each filling evokes a smooth rise of pressure which subsides, or "adapts," when the volume is maintained constant. The waves of pressure, which are quite distinct from the respiratory and other fluctuations of abdominal pressure, and only once related to a rise of rectal pressure (fig. 8 B), are undoubtedly of vesical origin and are waves of vesical contraction. At the higher volumes the waves emerge from the steadily mounting resistance of the bladder to distension. The subsequent adaptation of this resistance to any given volume, well seen in the graph, fig. 1, reveals the origin of the resistance in active vesical contraction evoked by distension. The resistance, when examined by brief fillings, gathers momentum up to a point, after which, whether filling is continued or not, there is a pause followed by the appearance of waves of vesical contraction (cf. fig. 8 C and 8 E). If filling is not interrupted the resistance usually mounts steadily and waves of pressure appear as soon as the resistance reaches its maximum (figs. 2 B and 9 D). The more rapid the filling the higher is the rise of tonic resistance for equivalent volumes (fig. 2 A). Emptying in small amounts does not disturb the rhythm of vesical waves (fig. 9 B), and if in large amounts lowers the pressure rapidly (fig. 9 C), and waves of contraction lessen rapidly in amplitude (fig. 9 E). No fresh vesical contraction was observed to be stimulated by emptying.

In Case 2 the curve of pressure rose more slowly as the volume increased (fig. 3) and approximated more closely to the normal. The pressure reached 18 cm. water at 400 c.c. during one filling. A regular series of small waves of pressure early made their appearance (fig. 10 A), and later appeared in groups (fig. 10 B and C) as in Case 1. Emptying the bladder had precisely the same effect as in Case 1.

In Case 3 the rise of vesical pressure was steeper (figs. 4 and 13 A) as in Case 1, reaching 29 cm. at 200 c.c. and 46 cm. at 300 c.c., but spontaneous fluctuations were only faint and occurred for only a short period at a volume of 200 c.c. during filling. They appeared also at

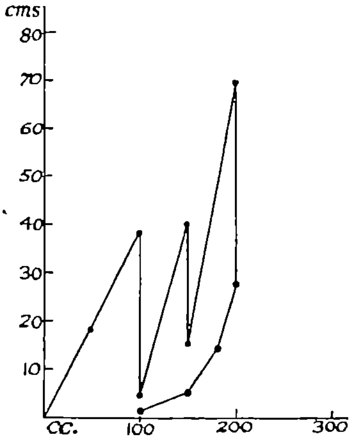

FIG. 1.

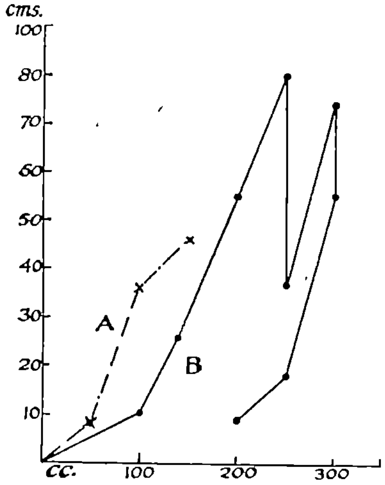

FIG. 2

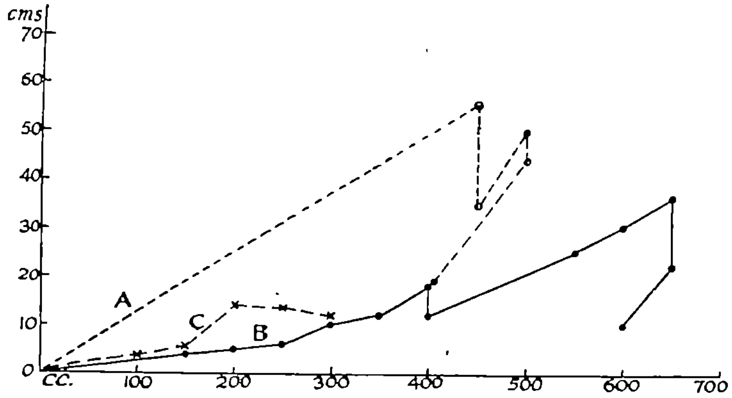

FIG. 3.

FIGS. 1 to 7.—Graphs of relationship of intravesical pressures and volumes plotted from continuous records during distension of the bladder. In figs. 1, 2 B, 3 A and B, 4, and 7A, the curve is continued backwards through the same volumes to show the pressure during subsequent emptying. Adaptation of pressure to a relatively steady value, whenever the volume was maintained constant for a period, is plotted as a vertical line.

FIG. 1. *Case* 1.—From records of slow filling, part of which is shown in fig. 8. Reservoir height 50 cm. to 100 c.c. and from then onwards 100 cm.

FIG. 2. *Case* 1.—Broken line A from record of very rapid continuous inflow at 100 cm. reservoir height. Fluid commenced to flow around catheter at 150 c.c. B, Graph of continuous inflow at intermediate rate at 100 cm. reservoir height. (See fig. 9 D.)

FIG. 3. *Case* 2.—From three different experiments. A, October 15, 1932. Continuous inflow with reservoir height 100 cm. B, November 13, 1932. Filling with reservoir height 50 cm. (See fig. 10 E.) C, November 27, 1932. Slower distension, reservoir height 100 cm. (Fig. 10 A, B, C and D.)

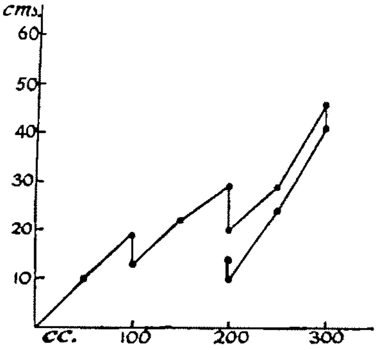

FIG. 4.

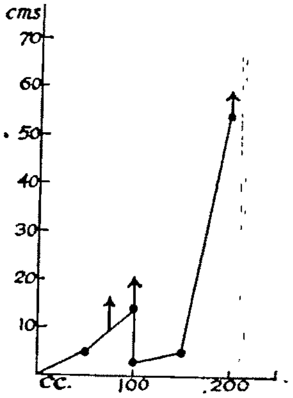

FIG. 5.

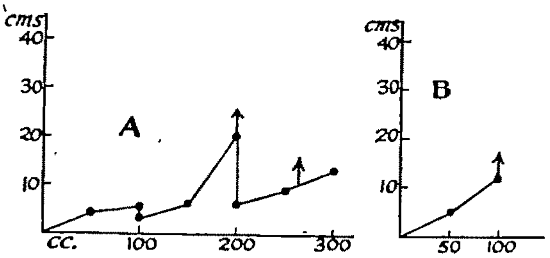

FIG. 6.

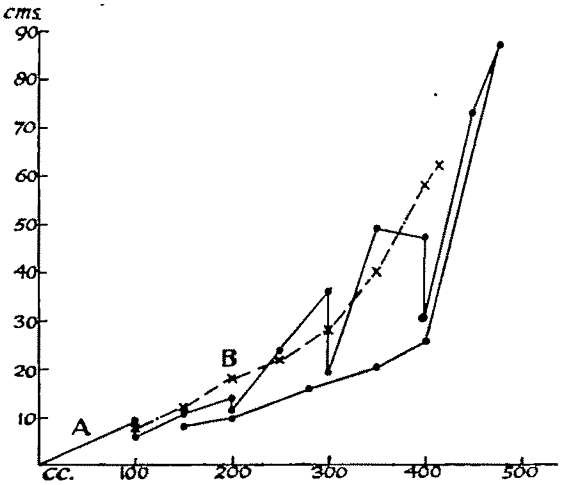

FIG. 7.

FIG. 4. *Case* 3.—August 27, 1933. Reservoir height 50 cm. Slow filling, part of which is shown in fig. 13 A.

FIG. 5. *Case* 4.—February 18, 1933. Filling to 150 c.c. at 50 cm. reservoir height and from 150 to 200 c.c. at 100 cm. reservoir height. Arrows represent the occurrence of isolated spontaneous vesical contractions. (See figs. 11 A, B, C and D.)

FIG. 6. *Case* 5.—A, May 29, 1933, 50 cm. reservoir height (fig. 12). B, August 29, 1933. Rapid filling. Reservoir height 50 cm. Immediately after inflow closed at 100 c.c. a large spontaneous contraction reached 130 cm. pressure.

FIG. 7. *Case* 6.—September 30, 1933. Continuous line A from record with reservoir height 50 cm. to 400 c.c., 100 cm. to 478 c c. (latter portion of record in fig. 13 E). Broken line B shows continuous filling at slow rate. Reservoir height 100 cm. (fig. 13 H).

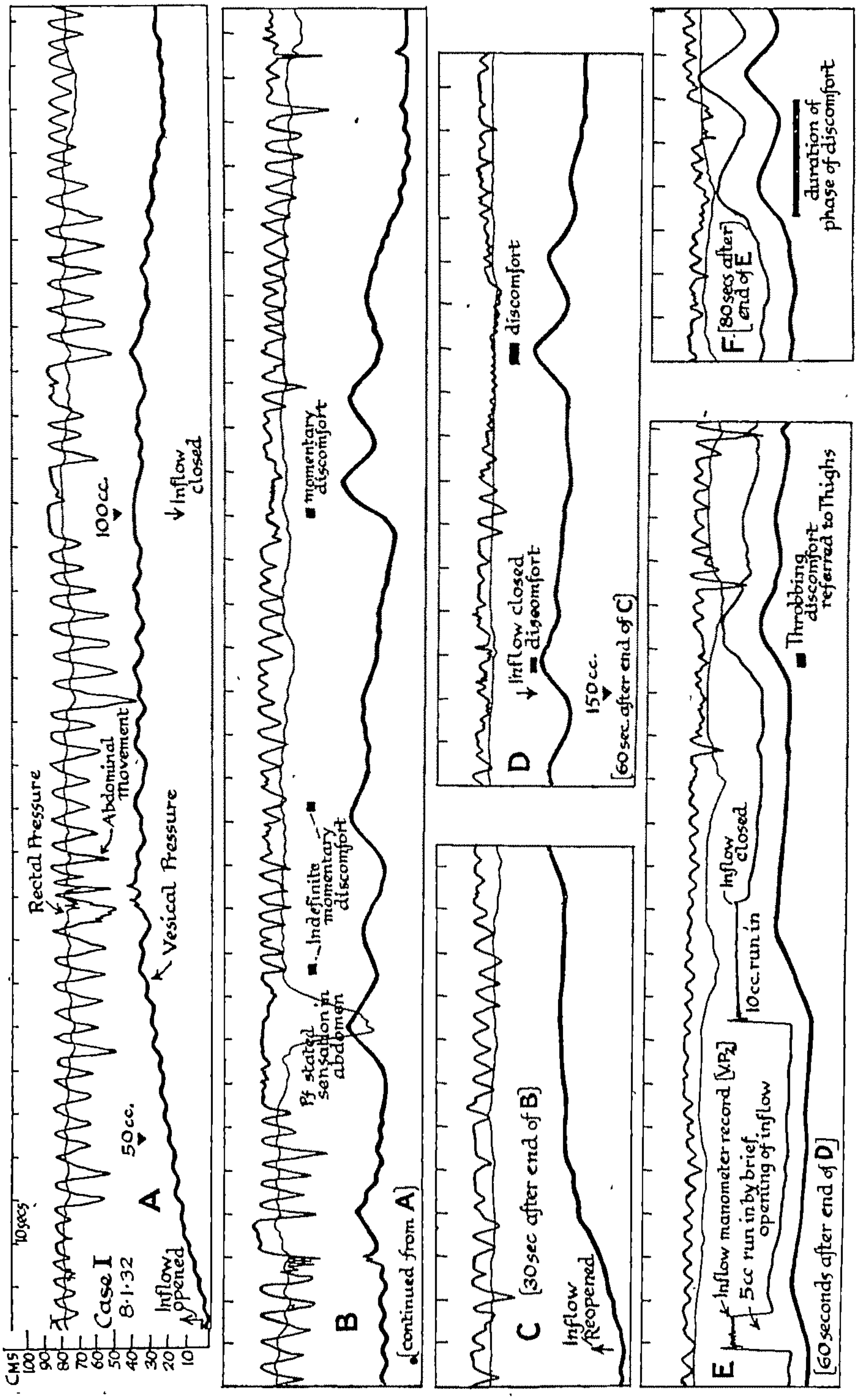

Fig. 8. *Case* 1.—Tracings from record of vesical pressure showing reaction to distension. Reduced to ⅗.

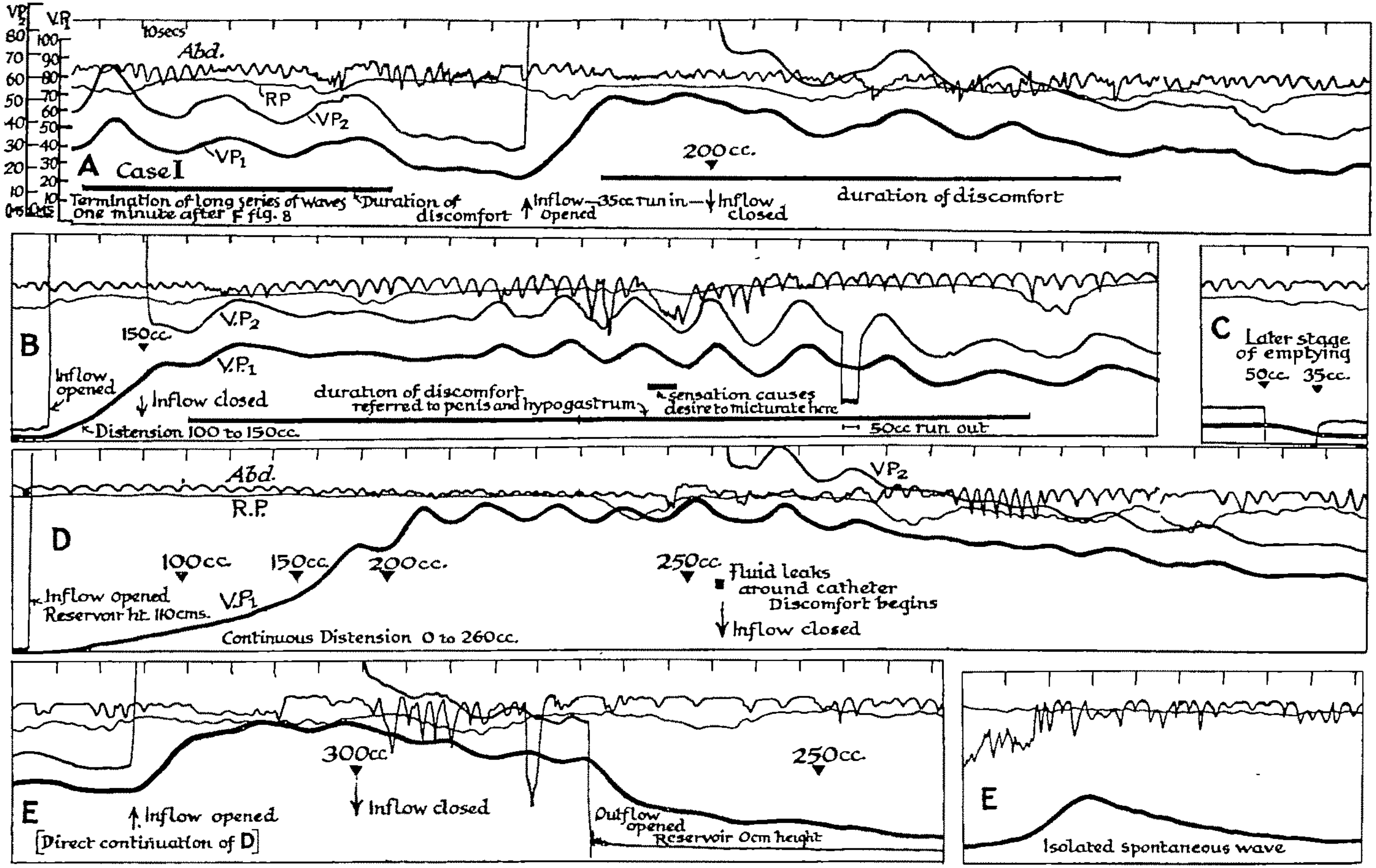

FIG. 9. *Case* 1.—Further excerpts from the same experiment as in fig. 8. A begins one minute after fig. 8 F. Volume in E 140 c.c.

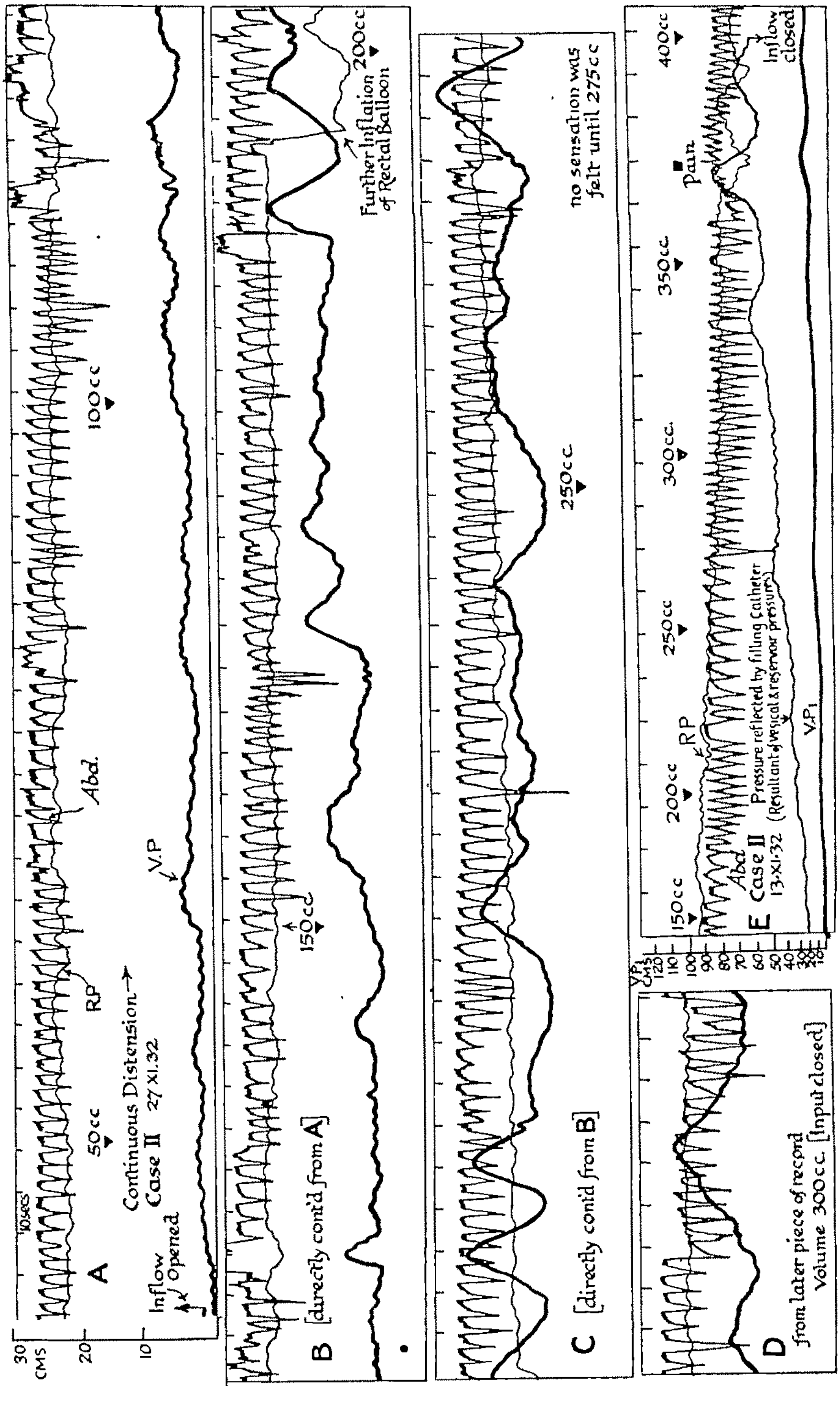

FIG. 10.—From records of Case 2. Vesical pressure during continuous distension.

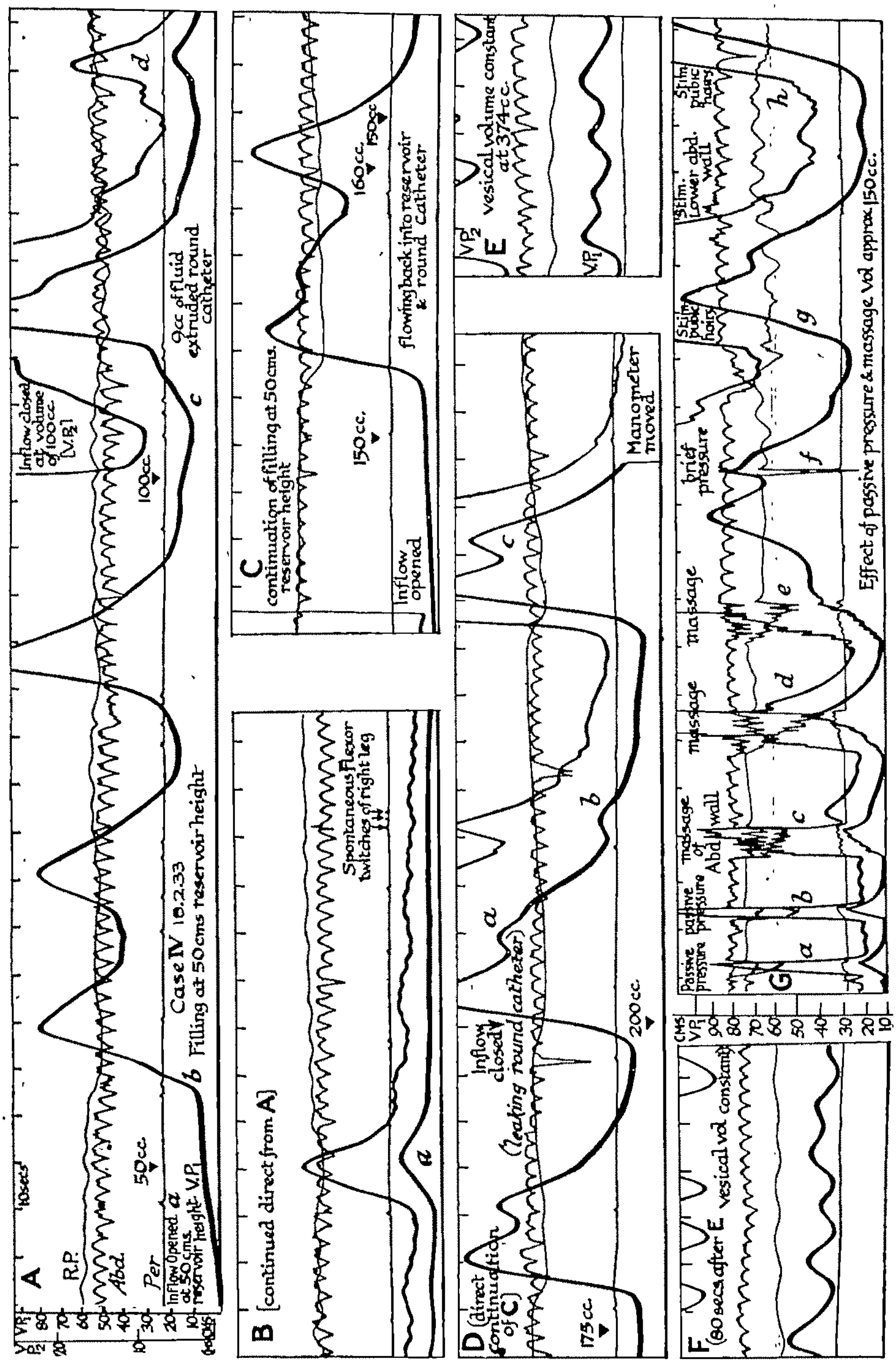

FIG. 11. *Case* 4.—A, B, C, D, E and F show reaction to intermittent distension. G illustrates effect of extravesical stimulation.

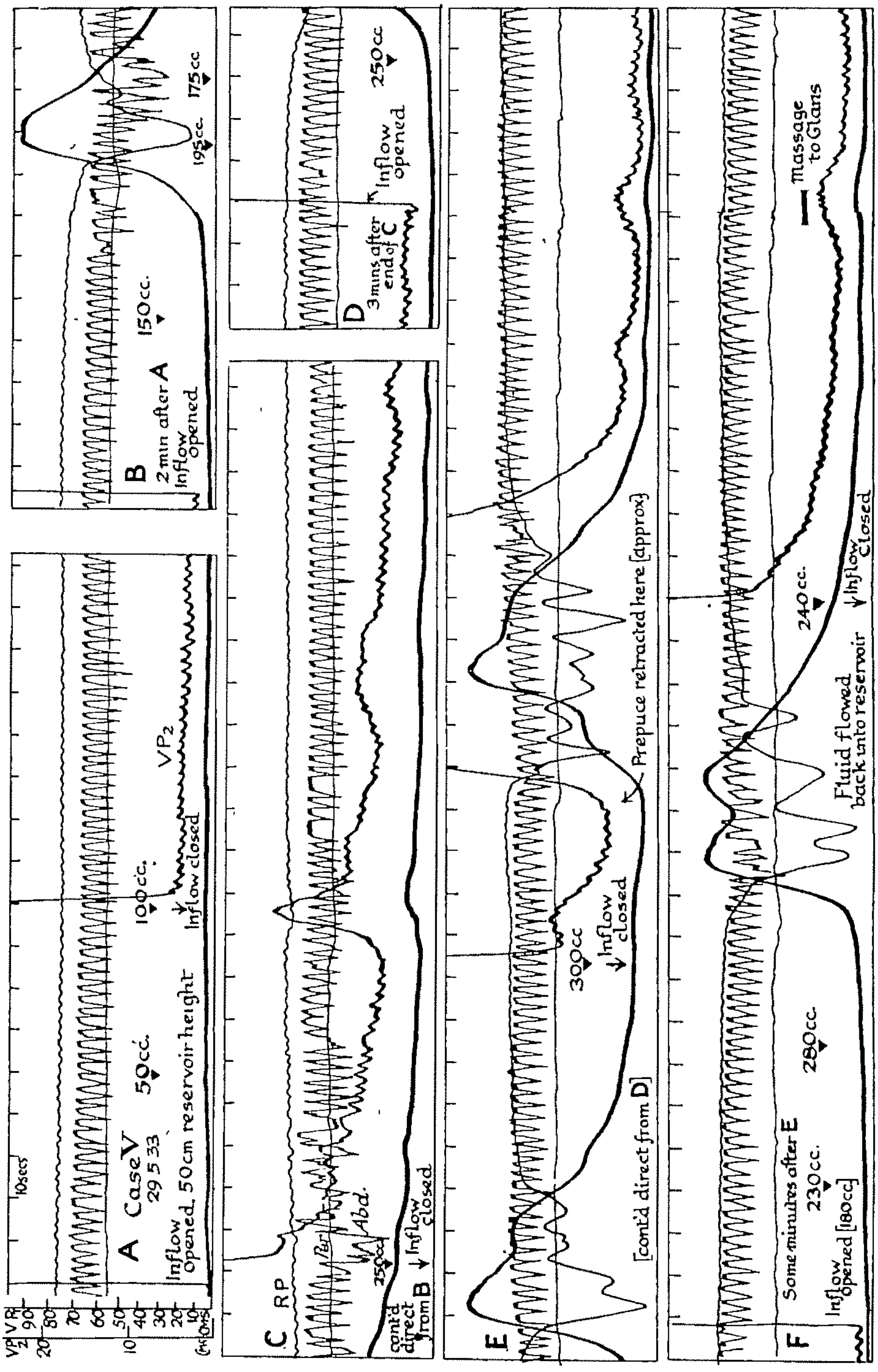

FIG. 12. *Case 5.*—Experiment, May 29, 1933. Records of reaction to intermittent distension.

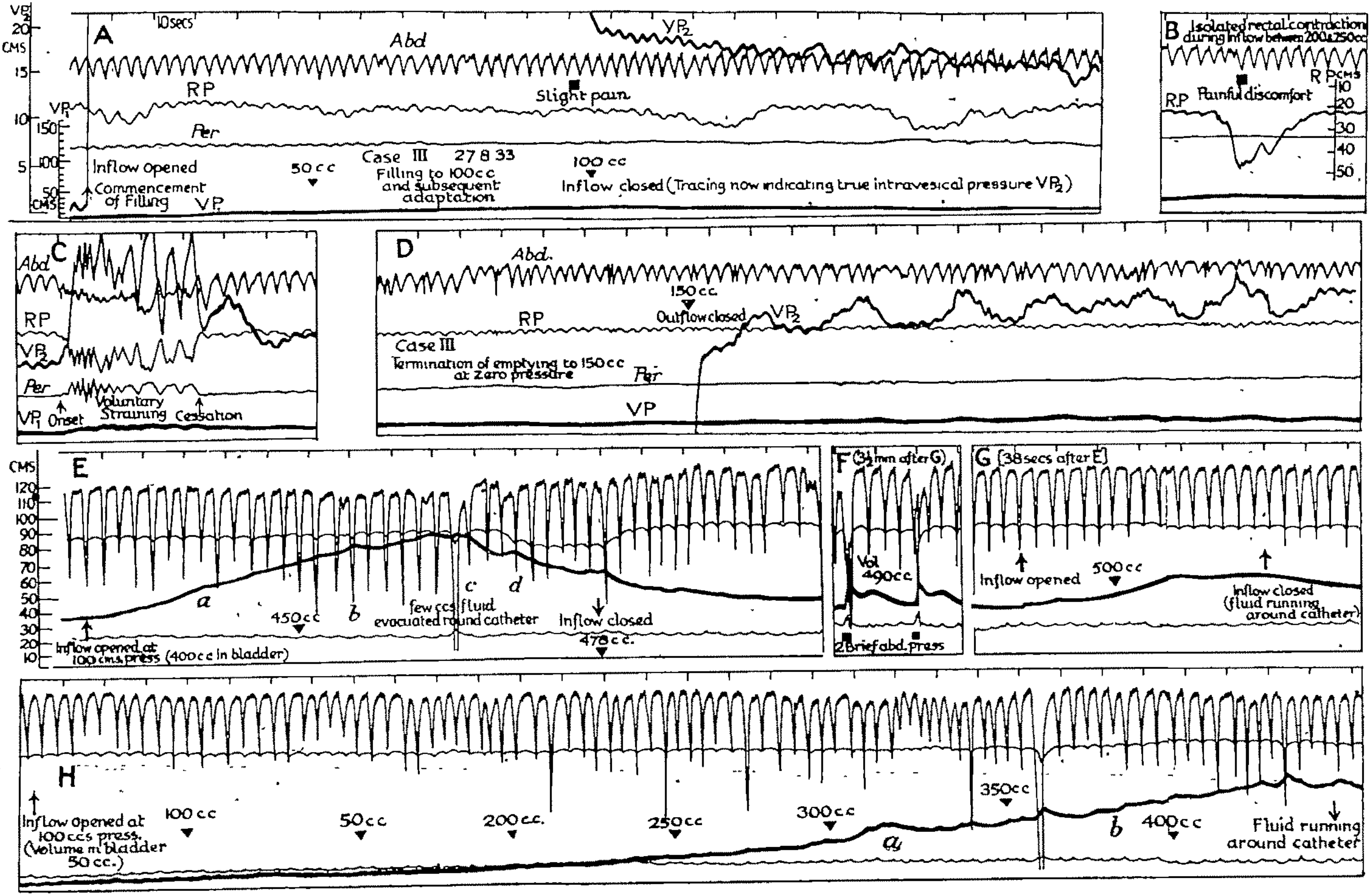

FIG. 13.—A, B, C and D, are excerpts from records of Case 3, and E, F, G and H from Case 6.

a volume of 150 c.c. (fig. 13 D), as the pressure rose following a period of emptying.

Variation in the manner of distension alters the reaction. For example, in Case 1 a continuous inflow, increased in rate by raising the reservoir pressure to 100 cm. water, induces a steeper pressure curve (fig. 2 A) than that obtained under our usual conditions (fig. 1), accompanied by similar though not earlier stimulation of spontaneous fluctuation. Refilling the bladder after a long period of distension at high volume gives a lower pressure throughout (figs. 3 B and 10 E).

In these bladders the process of adaptation of pressure to any constant volume is highly developed. In fig. 1 it will be seen that this resting value at each volume is often only slightly higher than the pressure at equivalent volume as the bladder is emptied. During the process of distension there is therefore evoked an increment of resistance of the vesical wall which is added to what may be taken as that due solely to the passive elasticity of the organ. This increased resistance to filling is the greater as speed of filling is increased. The manner and degree of its development strongly suggests an active tonic reaction of the bladder in response to *increasing* tension on the vesical wall, which commences to subside immediately the volume is kept constant.

A sudden passive rise of pressure such as is produced by a momentary pressure on the bladder through the abdominal wall in each of these cases is followed immediately, or at an interval of up to two seconds, by the onset of a small low wave of increased pressure (fig. 14). The pressure had to be rapidly applied as well as brief in duration. The reaction of the bladder to distension is thus "sampled" by a brief stretch, and is therefore revealed in phasic as well as progressive effect. This

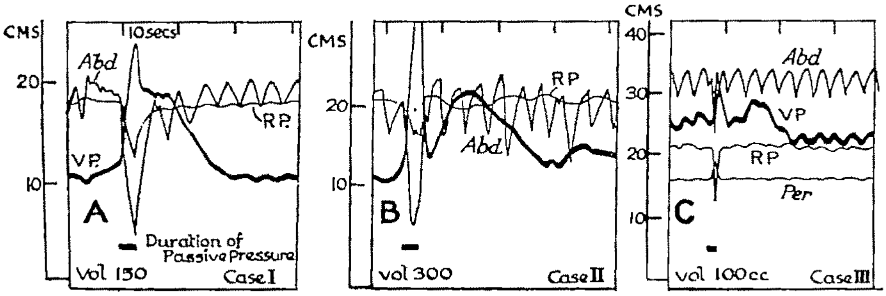

FIG. 14.—To show the vesical contraction stimulated by brief passive pressure on the bladder in each of the three cases of cauda equina lesions. The duration of the passive pressure is indicated by a horizontal black line. Reduced to ½.

delayed wave is also seen after the last of a series of pressures (fig. 13 c) but is not in the nature of a physical effect, for an equivalent or larger fall of pressure following upon a prolonged *steady* pressure never elicits it. The secondary contraction, as we shall refer to it, follows only brief pressure and is the result of some stimulus during the onset of the pressure.

The spontaneous waves of vesical pressure in this type of lesion were usually fluctuations of the same duration as the response to brief stretch, and we regard this as the single contraction of the bladder, analogous to the "twitch" of striped muscle. In Case 1 and Case 2 a larger, more prolonged wave, compounding several such small waves, appeared spontaneously at intervals (fig. 9 E). In Case 3 no such fused large contractions occurred. Apart from a rapid imposition of pressure upon the bladder through the abdominal wall, no external stimuli provoked any evidence of vesical activity.

### (2) *The Effect of Complete Transverse Lesion of the Spinal Cord.*

As with the bladders after lesions of the cauda equina we have not been able to examine the first stage of complete retention of urine. The following description applies to the stage of recovery of reflex activity by the divided spinal cord. The reaction of the bladder to distension was powerful in Cases 4 and 5. The vesical pressure, as may be seen from the graphs (figs. 5 and 6), rises steadily but only moderately steeply, to reach 5 to 14 cm. water at 100 c.c. In each case the process of filling appeared to excite remarkably powerful and prolonged contractions of the bladder, reaching over 100 cm. pressure (figs. 11 and 12) lasting some thirty to sixty seconds and relaxing to, or near, the preceding pressure although filling was continued. These large isolated responses occurred at volumes as low as 75 c.c. in Case 4 and 120 c.c. in Case 5. If filling were continued they occurred in a series at intervals of one to one and a half minutes (figs. 11A, *c* and *d*), but gradually grew smaller and less frequent as the volume became greater than 300 c.c. (Case 4) or 250 c.c. (Case 5), now giving way to a continuous series of small waves (fig. 11 E). These small waves at high volumes are of greater regularity and brisker frequency than those above described in the bladder after lesions of the cauda equina.

If the volume were kept constant after the appearance of a large wave, the disturbance was found to settle down slowly with the appearance of smaller waves in diminishing series (figs. 11 A, B and D, and fig. 12 C). The records of these waves at constant volume (isometric) reveal superadded smaller fluctuations, as in fig. 11 A at *c*, and 11 D at *a*, *b*, and *c*, and their persistence throughout the large wave on some occasions, and disappearance in the trough, is interpreted as evidence that the large prolonged responses are compounds of such small single waves, here imperfectly fused.

Diminution of the volume of vesical contents by releasing the outflow resulted in a steady fall of vesical pressure. If the outflow were rapid any contractile activity which was previously present disappeared forthwith; if slow both frequency and amplitude of contraction rapidly diminished. On no occasion did diminution of volume stimulate vesical contraction. The low pressure during emptying reflects only the passive elasticity of the organ. If the outflow were closed after discharge of any volume of vesical contents the pressure remained very low, approximating to that of the inactive bladder at that volume, and contractile activity gradually reappeared only after an interval.

The large isolated contractile reactions which form the prominent feature of the fillings of Cases 4 and 5 are evoked by distension of the bladder. The tension of such contractions appears to be in the region of the greatest of which the bladder is capable and for that reason we shall term them "maximal" responses. They may be likened to the motor tetanus of striped muscle. The introduction of small volumes of fluid reveals that a certain definite volume of increase is required to elicit them. For example, in Case 5, a contraction of this type having been allowed to subside, fluid was run into the bladder at high input pressure in varying amounts, and 7 c.c. and 14 c.c. were each unsuccessful. Though each was accompanied by a rise in the intravesical pressure this rise commenced to diminish as soon as the inflow ceased. On the introduction of 16 c.c., however, the vesical pressure rose more steeply with the last 4 c.c. and, despite cessation of inflow, mounted with increasing steepness to form the ascent of a large isolated wave of contraction. The resistance of either lumen of the double catheter being large, an especial experiment was devised for the sudden introduction of 1, 2, 5, 10 c.c. of fluid by means of a syringe and single catheter in subject 5. This manœuvre was ineffective in eliciting contraction even when 10 c.c. fluid was introduced within one second, or introduced and withdrawn within two seconds. The rise of vesical pressure corresponding to the introduction of 10 c.c. at an existing volume of 100 c.c. is small. It will be clear, however, that the reaction to distension is not so much a matter of volume as of increase of stretch. For example, it is seen in fig. 11 that though a maximal contraction was evoked by filling to 100 c.c. in

Case 4, if this were allowed to subside further filling elicits a maximal contraction only when the volume is approaching 200 c.c. (fig. 11 c). In Case 5 the same latency of reaction is found if one reaction were allowed to subside (figs. 12 D and F). The stimulus for the reaction is increment of stretch of the wall of the bladder.

In a different manner, probably depending upon the speed of acceleration of tension, a sudden stretch of the bladder evoked by a momentary passive pressure on the lower abdomen regularly elicits vesical contraction. This takes the form of a single wave of vesical pressure, commencing within two seconds after the onset of the brief stretch (fig. 15, and figs. 28 and 29, Plate XV). The duration of this contraction is that of the smallest spontaneous wave observed in the same bladder (fig. 29 B) and, as in the bladder after cauda equina lesion, we may regard it as a single or " twitch " contraction. It was found that an exceedingly brief, though powerful, pressure was not effective or produced only a very slight secondary contraction (fig. 29 A), whereas slightly longer pressures, reaching a maximum and declining to complete release in from 0·5 to 1·5 seconds, were the most effective (fig. 29 B). Provided that the pressures were gentle and sufficiently rapidly made the response varied in maximum tension, but not in duration, with the degree of pressure exerted (fig. 28). More powerful pressure, even if brief, induced a more delayed and flattened response (fig. 29 C), Slower pressures occasionally produced a similar wave of contraction but were more often ineffective (fig. 11 G). Repetition of passive pressure during the latent period, if light, appeared not to delay the

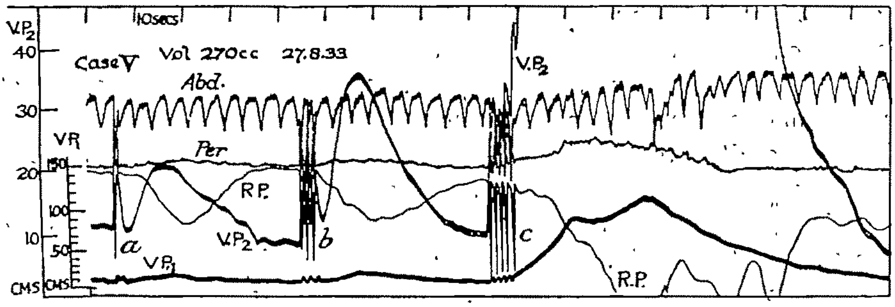

FIG. 15. *Case 5.*—To show the summation of the effect of repeated brief passive pressures on the bladder at constant volume. At *a* one brief pressure is applied and released, at *b* three, and at *c* five such pressures are imposed in rapid succession. The lowest curve (V.P.$_1$) shows the vesical pressure recorded by a manometer much less sensitive than that which gives the record V.P.$_2$. The rectal pressure (R.P.) also shows induced waves of rectal contraction. Reduced to ½.

appearance of the contraction, which was larger in proportion to the number of pressures applied (fig. 15). Heavier pressures were either without effect or delayed the phenomenon until after the last pressure of the series (fig. 28). More frequent repetition of pressure also impaired the development of contraction during stimulation. The response to brief stretch is thus much more readily elicited from these bladders and develops much greater tension than in those isolated by cauda equina lesions. Such increases of abdominal pressure which accompany a cough, a sigh, or a deep breath are effective in evoking this contraction wave with its characteristic latency. As in Cases 1, 2 and 3, moderate pressure suddenly applied, maintained for a period and then released, is not followed by any secondary contraction (fig. 11 G at *a* and *b*). The stimulus for the vesical contraction is the increase of pressure. The delay in appearance of the contraction after the last of a series of pressures, as in fig. 28, at *d* and *g*, therefore cannot mean that the contraction is stimulated by the fall in tension, but that it is the result of the last increase of pressure of the series. The earlier pressures in the series must also produce contractions which are impaired by subsequent stretch, but when the pressures seem to produce greater effect, as in fig. 15 at *b* and *c*, the tension is found to be already rising between the later pressures.

If the passive pressures upon the bladder were long enough repeated a large isolated maximal contraction, such as is evoked by filling, is readily elicited (fig. 15 *c*, fig. 28 at *a*, fig. 30 at *b*). The transition from small waves to large response is, however, not smooth, and the induced secondary wave, having reached a plateau or "step," fails to decline, and the tension commences to rise again, passing into a "maximal" response (figs. 28, 30). If the series of pressures were prolonged no transition was observed (fig. 33). The contraction directly induced by single brief passive pressure and by a short series of such pressures, appears of comparable size and ease of elicitation whatever the volume of vesical contents. The passage of such a contraction into a "maximal contraction" is facilitated by distension of the bladder and is readily provoked at volumes approaching that at which such a reaction tends to occur spontaneously. That volume is not, however, the only deciding factor in the appearance of the transition is revealed by the slight differences which decide its elicitation at a constant volume. In fig. 28, two contractions are induced by a series of light pressures, at *a* and *d*, the larger of which passes into a maximal contraction. Similarly, in fig. 30, of two similar contractions the greater, *b*, stimulated by slightly more intermittent pressure, leads to transition to a maximal contraction. A certain degree of active contraction must be stimulated before the transition will take place. Active contraction provoked by distension can replace in part that required to be produced by passive pressures, which then make transition to maximal contraction more readily. There was found every possible combination of the secondary effect of passive stretch and the active contraction produced by increasing volume. The maximal contraction at *e* in fig. 11 G is in fact identical in mode of production with that at *b* in fig. 11 A. In each case active contraction of the detrusor is brought to such a level that it appears to become self-stimulating and thus explosive.

Once a maximal contraction is elicited by this crisis of self-stimulation it does not persist, but disappears after a fairly constant period only to reappear after another period, so that rhythm occurs. It has been shown that continuous stimulation of the pelvic nerve in animals evokes a rhymical contraction of the detrusor [53]. The mechanism of rhythm production is here apparently identical with that of the heart and of spinal reflexes such as the scratch reflex or reflex stepping, and involves the little understood development of " refractory phase."

In Case 4, the more rapidly the bladder was filled the lower the volume at which a reaction occurred, a relationship well known to earlier workers [18]. This relationship was less prominent in Case 5.

The large explosive "maximal response" was in Case 5 invariably accompanied by a rise of rectal pressure which commences a few seconds later than the rise of vesical pressure (figs. 12 and 30). After mounting steadily, the rectal pressure then breaks into rhythmical fluctuations, showing partly fused small contractions at intervals of approximately ten seconds, and gradually subsiding as the vesical contraction passes away. The rise of pressure is not so prominent in Case 4, though waves of rectal pressure, of rhythm entirely different from abdominal and vesical movements, occur (figs. 11 G *g*, and 11 A *c*). Small rectal contractions were rarely observed and were elicited by brief pressures, very rarely as a delayed effect of abdominal pressure (figs. 15, fig. 28, and fig. 29 D at *a*). Isolated rectal contractions were also occasionally seen in Cases 1 and 2 (fig. 32 B).

Case 6, who was in a state of advanced toxæmia, exhibited a different response to distension of the bladder. The vesical pressure rose gradually to 16 cm. water at 200 c.c. (fig. 7) and small slow fluctuations appeared. The pressure rose rapidly at 300 c.c. and 400 c.c., but not until 450 c.c. was reached did a reaction with small superimposed spontaneous fluctuations occur (fig. 13 E). The pressure had mounted evenly to 73 cm. water and began to fluctuate (fig. 13 E at *a*, *b*, *c* and *d*), with escape of some drops of fluid around the catheter. After an interval, during which this reaction subsided, further filling evoked another similar reaction at a volume of 500 c.c.

These reactions presented a much more gradual transition from the tonic contraction of the bladder than did the high resistances of Cases 4 and 5, but fused waves were present. A brief pressure evoked no recognizable secondary contraction at volumes of 100 c.c. and 200 c.c., a small secondary contraction occurred after each pressure at 300 c.c., and a much more pronounced contraction at a volume of 400 c.c. (fig. 13 F). A series of powerful passive pressures upon the bladder did not succeed in inducing any larger response. The detrusor in Case 6, therefore, reveals the essential phenomena seen in Cases 1, 2 and 3, and lacks the large explosive maximal responses found in Cases 4 and 5.

## IV.—Disturbances of Function of the Sphincters.

### (1) *The Effect of Lesions of the Cauda Equina.*

The clinical disturbance of micturition complained of by the patients in this group was in two cases (1 and 2) an intermittent spontaneous passage of urine accompanied by an unpleasant sensation which caused the patient to attempt to assist its passage by straining. Both patients could usually commence micturition by straining. In Case 3 there was uncontrollable dribbling micturition increased by any bodily movement, and also ability to pass urine by voluntarily straining the abdomen. None of these patients was able to restrain a spontaneous micturition during its progress.

The method of registration of discharge from the sphincter was by withdrawal of a larger outer catheter until vesical pressure ceased to register, as we have described in detail elsewhere [15]. A leak was then allowed in the manometer system of the outer catheter so that a rise of pressure in the associated manometer tracing (labelled U.M. in illustrations) revealed the onset of discharge of fluid beyond the sphincter and also a fall of pressure immediately closure of the sphincter commences. The inner catheter remained within the bladder, and its manometer recorded the changes in vesical pressure (V.P. in illustrations).

Spontaneous micturition is readily evoked by increasing distension. Analysis of the records of Cases 1 and 2, in whom well-defined spontaneous micturitions were observed, reveals discharge of urine occurring during the course of spontaneous fluctuations of vesical pressure such as were observed in these bladders in the course of the reaction to distension. The discharge accompanied waves which were in every instance

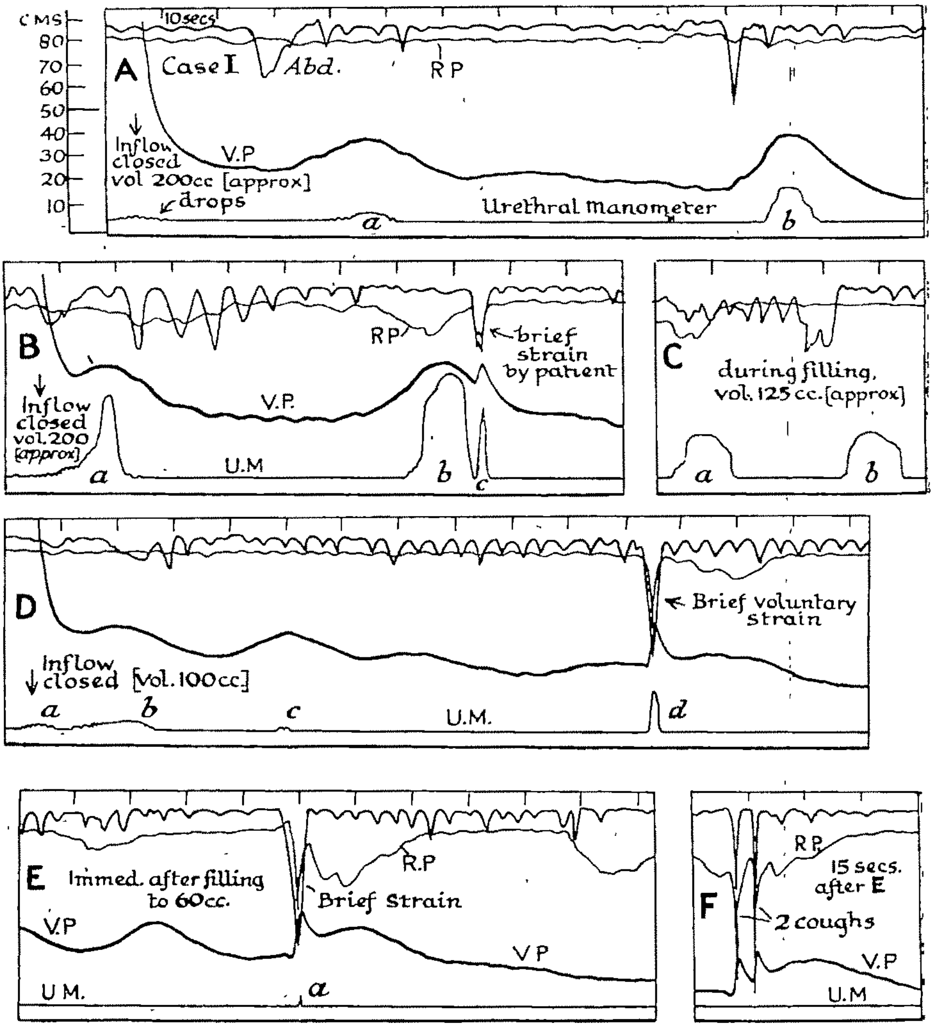

FIG. 16. *Case* 1.—Spontaneous micturition resulting from distension of the bladder. In records A, B and D the inflow was shut off as the first few drops of discharge were observed to pass through the urethral catheter, and from that time onwards true intravesical pressure is recorded by the manometer, V.P. The pressure of discharge is recorded by the urethral manometer, U.M. Reduced to ½.

longer in duration than the smallest waves during distension and longer than the waves induced by brief stretch. They were exactly comparable to the waves shown in figs. 9 E and 10 D. The sphincter opens at intravesical pressures varying from 24 to 30 cm. in Case 1 (fig. 16), and 18 to 23 cm. in Case 2 (fig. 18), and closes at a slightly lower value. At times the sphincter remained closed with a vesical contraction reaching a slightly higher pressure (e.g., 31 cm.) than that at which it had opened just before (e.g., 27 cm.). The closure of the sphincter occurred at a vesical pressure just above that at which it had opened. Commencement of discharge is gradual, with early acceleration, so that the later part of the opening may be abrupt (figs. 16 B, C, and 18 B). The main portion of discharge reflects the pressure of the accompanying vesical contraction. Closure of the sphincter shows the same sinusoidal curve as is seen in its opening, and the discharge is often symmetrical. On some occasions the sphincter opened gradually but closed in a more decisive fashion (fig. 16 B, *a*). The commencement of spontaneous discharge was always secondary to a spontaneous rise of vesical pressure of wave form.

Accompanying many responses a respiratory arrhythmia of much longer duration, with little resultant change in intra-abdominal pressure, revealed the tendency of the patient to make straining movements of the abdomen to hasten micturition in order to attempt to abolish the unpleasant sensations arising with the spontaneous vesical contractions. The patient found it difficult to suppress this movement. The intra-rectal pressure curves show only the sporadic changes which continued independently of micturition and were not modified by its occurrence.

In Case 3 no defined automatic evacuation of fluid occurred during experiment. Although spontaneous waves of vesical contraction occurred at intervals they were of small amplitude and duration. At a vesical volume of 200 c.c. fluid escaped past the sphincter in a continuous series of drops at intervals of approximately five seconds. There was no large accompanying fluctuation of vesical contraction. The manometer used in recording vesical pressure at this time was not sufficiently delicate to establish the presence or absence of the small waves of vesical pressure seen during distension in this patient.

When Cases 1 and 2 were instructed to attempt voluntary micturition the intra-abdominal pressure was raised by voluntary contraction of the diaphragm and abdominal wall. The rectal and vesical pressures rose steeply (fig. 17, fig. 32 A, C, D, E and fig. 18 D at *a*). Discharge commenced when the vesical pressure had reached 27 to 53 cm. of water in Case 1, and 26 to 28 cm. in Case 2. The higher the vesical pressure immediately before the effort the lower was the pressure at which the sphincter opened during the effort. The decline of the pressure of discharge following a rapid cessation of straining was usually at first gradual, with delayed sharp closure of the sphincter, well marked in the first discharges in fig. 17, at other times an abrupt cessation with the first lessening of abdominal pressure. When Case 3 was instructed to attempt to micturate he responded by voluntarily increasing his abdominal pressure, and here the record of pressure in a balloon applied to the perineum shows by separate manometer a forcible bulge of the flaccid perineum downwards (fig. 31). The outflow commences gradually and lessens in volume immediately the straining is lessened, to cease abruptly a brief interval after the cessation of the straining movement.

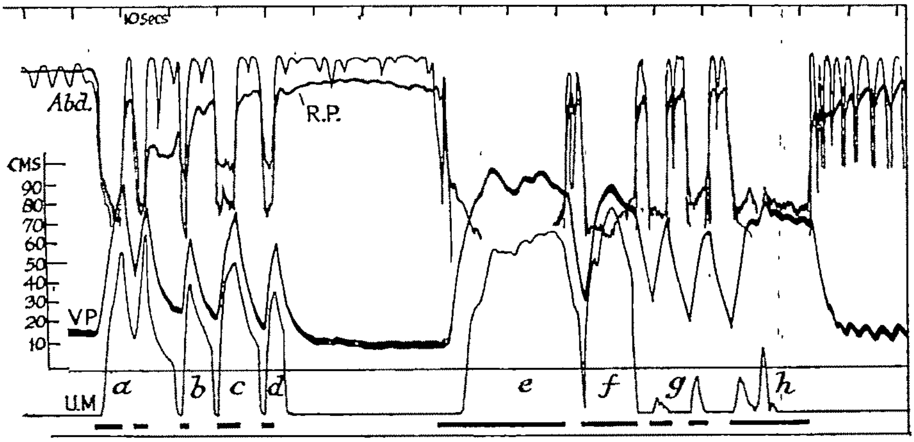

FIG. 17,—To show voluntary micturition by contraction of the abdomen and diaphragm ("straining") in Case 1. The duration of each such voluntary strain is indicated by the horizontal black lines at the bottom of the figure. In order to clarify the figure the records of vesical pressure and urethral discharge have been displaced vertically with due attention to time relationship. Reduced to $\frac{3}{7}$.

The delay in the fall of outflow pressure is related in all three cases to some delay in the fall of the vesical pressure, not so clearly seen in the records from Cases 1 and 3 as in some records from Case 2 (figs. 18 C and 32 B), and taking the form of a small late induced wave of vesical pressure. In all three cases a similar strain when the vesical pressure was registered by a more sensitive manometer and wider catheter was immediately followed by a brief induced wave of vesical pressure (as in fig. 14). The longer the duration of the strain the less obvious were both this subsequent induced wave and the delay of closure of the sphincter (fig. 32 E). There is evidence, therefore, that the delay in closure of the sphincter is directly related to the presence of vesical contraction in all three patients. A prolonged effort to pass urine by straining succeeds in maintaining discharge only for a brief period, after which any slight relaxation of the effort is accompanied by a jerky closure of the sphincter (fig. 32 D), with renewed discharge on further effort. Eventually the discharge ceases in spite of continuation of the effort, and still far short of complete evacuation of the bladder. After a very brief rest further effort could secure renewal of discharge and the bladder could be completely emptied by means of a series of repetitions of straining (fig. 17).

Pressure upon the abdominal wall of any of these three patients succeeded in expressing fluid through the sphincter. The vesical pressure at which discharge commenced was constantly higher than that at which discharge commenced when the patient made a voluntary strain (e.g., in Case 2, 26 to 32 cm., and in Case 3, 48 to 75 cm.), but this difference is partly, if not wholly, dependent upon the manner the vesical pressure is passively increased. It is not possible, without risking damage to the viscera, to apply powerful manual pressure so rapidly as the wide piston movement of the diaphragm effects. The more rapidly pressure is passively applied, and the more jerky the pressure at its maximum, the more effective it is in securing discharge, and it is in these factors that manual compression of the abdomen fails to make complete imitation of voluntary strains (cf., *a*, *b*, with *c*, *d*, fig. 32 A). The discharge induced by manual compression is in every other way identical with that provoked by voluntary effort. The delayed closure is exactly comparable in form and extent (fig. 18 D at *f*). A brief pressure upon the abdomen did not alone suffice to provoke discharge in any of these patients, and likewise a cough did not cause any discharge from an inactive bladder.

It was noticeable in all three cases that the effect of abdominal pressure or of a strain by the patient was profoundly influenced by the state of the vesical pressure immediately preceding the induced pressure, whatever the volume of vesical contents. If the pressure had been low, a high passive increase is without effect in provoking discharge (figs. 32 A 16 F). With intermediate previous pressures discharge is more readily provoked by lesser effort (fig. 32 C), and when vesical contractions are in progress (figs. 16 E at *a*, 16 D at *d*), and especially if spontaneous discharge has just occurred (fig. 16 B at *c*), the slightest applied pressure opens the sphincter. Passive pressure thus used as a test of the resistance of the sphincter reveals that spontaneous detrusor contraction, both in the form of waves and in maintained tonic contraction, is accompanied by laxity of the sphincter. The degree of laxity of the sphincter is directly proportional to the degree of active vesical contraction, both during actual discharge and during vesical contraction without discharge. When active detrusor contraction is slight or absent the sphincter is firmly contracted. We may apply this finding to the explanation of the delayed closure of the sphincter following passive pressure on the bladder. The small induced wave of vesical pressure, though in other circumstances not sufficient to be accompanied by discharge (as in fig. 16 F), here combines with the declining remainder of the passive vesical pressure to maintain patency.

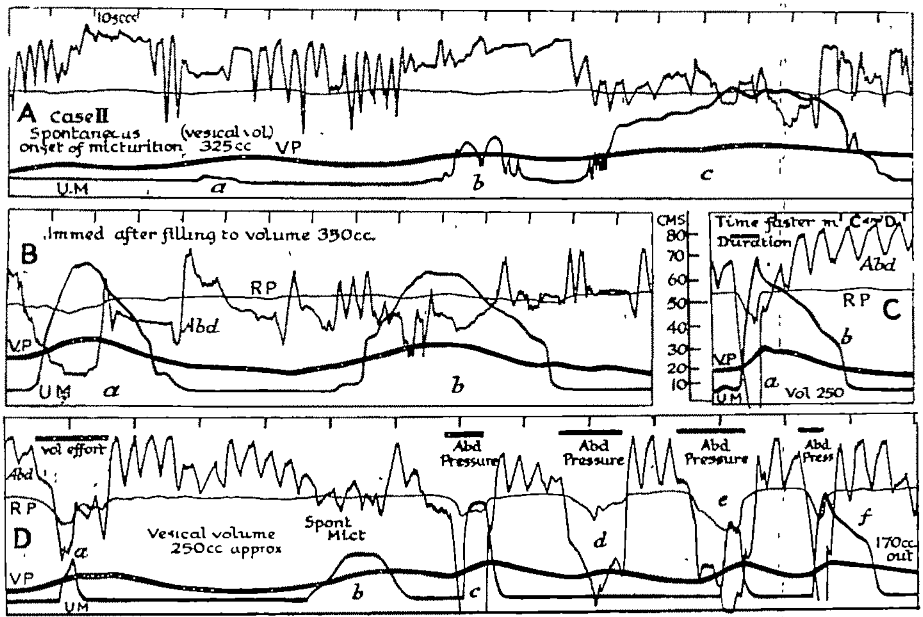

FIG. 18. *Case* 2.- The record A shows the gradual development of spontaneous micturition at constant volume in the absence of any extraneous stimulating factor. The even curve of rectal pressure excludes the respiratory arrhythmia from any direct relationship with the form of the micturition. In B is shown rhythmical discharge induced by distension at moderate rate. In C a voluntary strain at *a* induces discharge, and a continuation of the same piece of record in D contrasts the effect of passive pressure through the abdominal wall. The tension scale attached to C applies to the vesical pressure (V.P.) in all records. Reduced to $\frac{3}{5}$.

Attempts by these cases to obtain micturition by voluntary relaxation of the perineum, as is attained by the normal [15], were without influence upon vesical pressure. No vesical waves appeared and no relaxation of the sphincter or perineum occurred. An order to restrain micturition had no effect on detrusor tone, or on discharge when that occurred, and did not hasten the delayed closure of the sphincter. Only in Case 2 was there evidence of involvement of the upper lumbar nerve roots in the lesion. Presumably, therefore, the hypogastric innervation in the two other cases was intact, but could not be activated by effort of will. It is possible that the difference in opening pressure between an active strain by the patient and a passive pressure upon the abdomen by an observer is related to some voluntary effect via the hypogastric nerves. Such an effect was not observed to occur alone, and in the absence of change in vesical contraction, or independent closing or opening of the sphincter produced by it, we prefer to regard the difference as a purely mechanical one.

Withdrawal of the catheter so that it lay some 10 to 12 cm. distal to the internal sphincter made no change in the form of discharge. We were unable to find any evidence of a functioning external sphincter in these cases. Efforts to "hold hard" produced either no withdrawal of the perineum, such as we have described in the normal subject [15], or sometimes only slight withdrawal directly related to a fall in intra-abdominal pressure, due to inspiration. The only effect upon the flow of discharging urine was that induced by the fall of pressure with the manœuvre and directly reflecting the fall in abdominal pressure. In none of these patients had plantar stimulation any effect on vesical pressure, sphincteric discharge or perineal posture, where the latter was recorded. The external sphincter shares the flaccid paralysis of the remainder of the perineum.

During spontaneous vesical activity the internal sphincter reacts by relaxations reciprocal with the intensity of contraction of the detrusor, and during a series of waves this is very striking (figs. 16, 18). Cases 1 and 2 may be considered as typifying the automatic micturition following complete sacral lesions, whether by affection of nerve roots or of the conus medullaris. The innervation of the bladder by means of the sympathetic nervous system, though capable of effecting contraction of the internal sphincter when stimulated directly [38], is not available for voluntary effects, just as reflex micturition cannot be served by it in the cat, as was shown by Stewart [51].

In Case 3 there was an improvement from the initial retention of urine, but analysis proves it to be largely a mechanical micturition. The detrusor here has regained some spontaneous activity in the form of reaction to distension, both sudden and gradual, and possesses feeble rhythmical activity. The internal sphincter, more lax than in the state of retention, allows straining to force it mechanically (fig. 31). There is a clinical history of the development of this laxity, which was contemporaneous with the change from retention to dribbling incontinence.

We have shown that laxity of the sphincter is related to the coincident active contraction of the detrusor in Cases 1 and 2, and in Case 3 we may relate it to the same process.

Six months after the time of the experiment in Case 3, voluntary effort was completely lacking, and apart from a rather more brisk reaction to distension and a slight sensation from catheterization, was identical with that here described. We have no doubt that the activity here described is devoid of central effects. The long interval during which this patient failed to establish automatic micturition calls for comment, and we feel that the inflammatory nature of this lesion and its probable extension to the autonomic plexuses hold the explanation of the failure of automatic micturition.

### (2) *The Effect of Transverse Lesions of the Spinal Cord above the Sacral Segments.*

Three patients (Cases 4, 5 and 6) suffered from a variety of "active" clinical incontinence associated with reflex activity of isolated segments of the spinal cord. This incontinence occurred spontaneously in intervals of complete rest, in response to the gradual distension of the bladder by urine. The slightest movement of the patients, provided a flexor spasm was not invoked, often promoted micturition within three or four seconds, even if the bladder were only moderately distended. No micturition occurred with moderate flexor spasms (involving the abdomen in Cases 4 and 6), but *after the subsidence* of a severe flexor spasm or induced flexion, micturition tended to occur if the bladder were already distended. In Cases 4 and 5 a well-defined forceful automatic micturition was readily facilitated by the swabbing of the penis preparatory to catheterization. In all cases, including Case 5, in whom no reflex flexion was obtainable, clinical observation of the effect of a scratch to the sole of either foot revealed immediate complete suppression of micturition when that had been commenced by other means. After this sudden cessation of flow, discharge would rarely recommence, or only after an interval sufficient for the motor effects of the stimulus to subside. Cases 4 and 5 showed turgescence which subsided immediately micturition was elicited. We were not able to bring about erection by stimulation.

Our experiments succeeded in differentiating between two distinct closing mechanisms which we have reason to believe were the internal and external sphincter.

*The internal sphincter.*—When we had made observation of the effects of distension of the bladder with both catheters recording vesical pressure, the two were very gradually withdrawn until the manometer of the larger catheter abruptly ceased to show the respiratory fluctuations which characterize vesical pressure. If the outlet tap of the apparatus connected to this catheter were opened partially, no discharge of the fluid occurred, though its outlet lay below the level of the symphysis pubis. The catheters are then held rigidly at this level and vesical contractions are induced. The resulting discharge from the sphincter is poorly defined in both onset and cessation (Case 4, fig. 33, Plate XV, and Case 5, fig. 34, Plate XVI). The vesical pressure shows the origin of the disturbance in one of the "maximal" isolated contractions resulting from distension in these two patients. The pressure at which opening and closure of the sphincters occurs is low. Indeed it is often difficult to be sure that the urethral catheter is out of the bladder. When the micturition is provoked by massage of the abdomen, as in fig. 33, the sphincter is at first unaffected by the passive increase of pressure, but later allows the passage of a few drops between each increase, and swings open only as massage ceases and vesical contraction is in progress. Steady increase of passive pressure on the abdomen secured discharge only if active vesical contraction were in process. The pressure in the posterior urethra required to force the sphincter in the absence of active vesical contraction is moderate (35 cm.). Plantar stimulation (fig. 33) influences the discharge only in the slight fluctuations of pressure which, through the vesical pressure, reflect the abdominal movement which such stimulation induces. Records from Case 6, fig. 35, reveal the same characteristics, although here the vesical contraction is of very low amplitude, and the resulting discharge is poorly defined.

Strong passive pressure on the abdomen may cause a drop of fluid to pass the sphincter at the maximum of pressure, but does not secure wide opening or sustained discharge unless the rise of vesical pressure is sustained after the release of the pressure. The sphincter opens spontaneously only in the presence of a wave of vesical contraction, and its opening and closure are related to the ascent and decline of such vesical waves. It showed no rhythmical or other activity unrelated to contraction of the detrusor. Sharp closure at high vesical pressures such as has been observed in the normal internal sphincter [15] has not been seen, though smaller sharp closure occasionally occurs, as in the last response in fig. 33.

In Case 6 the internal sphincter was much more readily forced by passive pressure than in Cases 4 and 5, and the appearance of a further few drops after an interval reveals the presence of secondary contraction (fig. 36). When the volume was increased gradually the internal sphincter dribbled periodically in small amounts (1 to 10 c.c.) when 400 c.c. or more had entered the bladder.

*The external sphincter.*—If the urethral catheter is moved further distally for some 2 to 5 cm. the discharge during micturition is interrupted by plantar stimulation or involuntary flexor spasms. The characteristics of the discharge are altered; it commences abruptly (Case 4, fig. 38, Case 5, fig. 19), is liable to sudden lapses, complete and incomplete, and terminates in a sudden sharp fall. The pressure of the fully developed discharge varies with the vesical pressure. The pressure at which discharge commences and terminates is much higher than in the case of the internal sphincter alone. The opening and closure are frequently stammering in nature. The sudden lapses in discharge often correspond with sharp movements in the perineum, each of which leaves a small but rapid flicker in the perineal record (*a* in fig. 38, and *a*, *b*, *c*, *g*, and *h*, in fig. 39). These movements are due to perineal contractions, each corresponding to an involuntary flexor spasm. Their amplitude varied widely, and sudden complete cessation of vesical discharge was occasionally initiated by such a contraction.

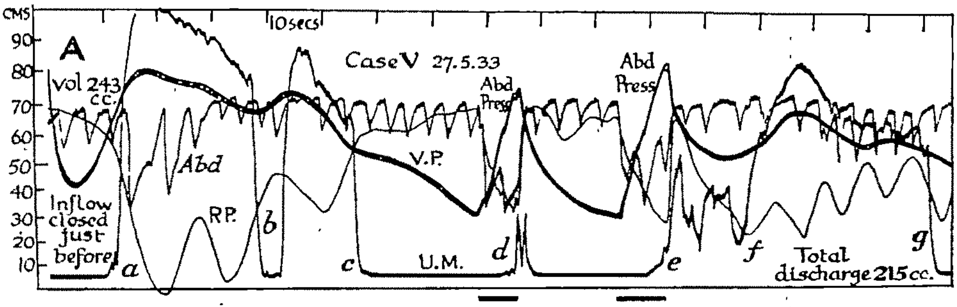

FIG. 19. *Case 5.*—To show spontaneous micturition induced by continuous inflow of fluid into the bladder, which ceases just as the figure begins. The spontaneous discharge past both sphincters is indicated by the urethral manometer U.M. After its cessation at *c* abdominal pressures (durations indicated by horizontal black lines) cause slight discharge at *d* and *e*, and eventually renew spontaneous discharge from *f* to *g*. The tension scale calibrates the vesical pressure (V.P.). Reduced to ½.

In Cases 4 and 5 discharge occurred only with large maximal responses. If, however, these were prolonged and showed smaller superimposed waves, discharge ceased abruptly during the troughs of some waves (fig. 19 at *b*, and fig. 39 at *f*). The pressure of discharge mirrors the vesical pressure, showing only the direct transmission of the latter through the widely open sphincter.

Micturition in Case 5 was invariably accompanied by rhythmical contractions of the rectum (figs. 19, 34, 44) and these were also often seen in Case 4, though here the rhythm was not usually so apparent (figs. 33, 38).

The external sphincter in Case 6 allowed discharge with smaller vesical contractions and these discharges were of the same small dribbling character as through the internal sphincter. A sudden closure rarely occurred (fig. 37). Spontaneous diphasic interruptions were frequent. The external sphincter in Case 6 could be readily forced by passive pressure on the bladder.

Stimulation of the sole of the foot provokes an abrupt cessation of discharge (figs. 41, 42, 43 and 44). The latency following stimulation is very brief (within one-tenth of a second after a single prick). The pressure of discharge shows a slight upward jerk followed by steep decline, and accompanying this diphasic movement there occurs a sudden jerky movement of the abdomen, a rise in the rectal pressure, and a downward bulge of the perineum by the increased abdominal pressure (figs. 39, 40, 41, 42). The vesical pressure shows a small steep rise followed by an equally steep decline (figs. 41 *b*, 40 *a*, and 45 *a*). After an interval of complete closure the sphincter opens abruptly, with often a small downward initial flicker. This diphasic type of closure of the external sphincter has been observed in normal men [15], and is interpreted as the result of the sudden powerful contraction of a muscle over a small length of the urethra to express any fluid it contains, and thus produces the initial upward jerk. The brief latency of the cessation of outflow can be explained only by contraction of striped muscle.

In Case 5 this type of closure was also present, but was frequently incomplete after a single prick, though it could be made complete by a more prolonged stimulus such as a scratch of the sole (fig. 44) or a series of pricks in rapid succession. The same phenomenon was observed in Case 6 (fig. 43). The effect in all patients outlasted a single stimulus by a very brief interval only.

Pricks to the glans penis also caused abrupt diphasic closure of the external sphincter (figs. 45, 52, 53 and 54) ; repetition (summation) was necessary to achieve prolonged arrest of discharge. If no discharge were occurring the sphincter did not open in response to such a stimulus, even if vesical contraction were in progress (figs. 40 *d* and 42 *c*), but a small flicker in the manometer shows that the contraction in the perineum disturbed the urethral catheter opening. The external sphincter was at this time closed, as a test subsequently described will demonstrate.

The small steep ascent of vesical pressure accompanying sudden closure of the external sphincter is more obvious if the previous outflow has been voluminous and vesical pressure rising (fig. 40 *a* and fig. 45 *a*). This is referable to the sudden jar to the shortening detrusor caused by abrupt arrest of the escape of the contents. The contracting detrusor abruptly meets resistance. If the outflow is constricted so that little fluid passes and micturition is prolonged, the increase is less sudden and smaller (fig. 39 *d* and *e*). This has also been observed in the normal bladder [15]. The sudden "jar" does not appear to stimulate further contraction of the detrusor, and the pressure commences thereafter to decline, often very rapidly. If a brief stimulus falls early in a powerful micturition there is immediate resumption of discharge after cessation of the stimulus. Reflex closure of the sphincter is more brief if induced before or during the initial peak of the vesical contraction, but if it occurs later it frequently is followed by decline of the micturition (fig. 40). If the closure of the sphincter is prolonged and the vesical contraction has fallen low in the interval the renewal of discharge depends on the height of vesical pressure (cf. figs. 40 *c*, and 41 *c*).

A rapid pressure to the abdomen during discharge of urine causes a sudden rapid increase of output pressure (by direct transmission) followed by abrupt lessening of discharge for a brief interval. The sudden tension on the contents of the urethra appears to stimulate closure of the external sphincter. As with the internal sphincter alone, expression of fluid by passive pressure on the abdomen is difficult when no vesical contraction is present, and easier the greater the degree of existing vesical contraction. Rhythmical pressure (massage) was the most efficient method of inducing micturition; it did so by exciting active vesical contraction (figs. 19, 38, 41, 44 and 45).

In order to determine the manner of closure of each sphincter, and their relationship in time when both were allowed to function, we withdrew the catheters so that the proximal narrow catheter lay between the two sphincters and the wider catheter lay distal to the external sphincter. Both catheter systems are allowed to leak so that cessation as well as the onset of discharge is shown. When micturition is promoted by abdominal massage the manometer of the proximal catheter records a gradual rise of pressure for some seconds before the external sphincter swings suddenly open (fig. 47 at *a*). The external sphincter closes more abruptly and earlier than the internal sphincter at the termination of discharge. During discharge thus caused, plantar stimulation (fig. 47 at *b*) causes the usual diphasic jerk and complete closure of the external sphincter. The catheter in the posterior urethra shows a rise of pressure and then a gradual decline, but does not close until vesical pressure has reached a low level. An involuntary spasm of flexion has the same effect. In recovery from brief closure the internal sphincter opens before the external if vesical contraction is maintained. Fluid introduced into the posterior urethra by means of the proximal catheter failed to pass the external sphincter or provoke its relaxation, but flowed readily back into the bladder when the reservoir pressure was greater than some 35 cm. water (Cases 4 and 5). The external sphincter therefore presents a maintained tonic contraction, whether there was spasticity below the level of the transverse lesion (Case 4) or when the tone of all other voluntary musculature was diminished or absent, as in Case 5. Vesical contraction is the only effective stimulus for its relaxation, and it occurs secondarily to that of the internal sphincter. Once relaxed in the course of a micturition it could be immediately and forcefully closed by peripheral stimulation. Spontaneously occurring flexor spasms were accompanied by variable degrees of partial or complete closure of the sphincter. The irregular jerkings of perineum and sphincter due to "flexor spasms" may at times cause rapid stammering, as in figs. 38 *a* and 39 *c*. A sudden increase of vesical pressure, such as that which accompanies sudden abdominal pressure, during micturition may cause closure of the sphincter, but vesical pressure may be unaltered by a weak flexor spasm or reflex flexion which nevertheless secures complete and lasting closure of the sphincter; closure is therefore a direct effect. The internal sphincter may be readily forced by passive increase of vesical pressure. Its lax condition reciprocates with the heightened activity of the detrusor. The resistance to catheterization of Cases 4 and 5 is due to the maintained activity of the external sphincter, the reflex control of which will be discussed below. In Case 6 both sphincters were less tonic, but although the limb reflexes were well developed, movements of the perineum and anal sphincter were weak.

The apparently invariable reciprocal relationship between the detrusor and internal sphincter suggests a fixed anatomical relationship such as would be provided by bifurcation of axis cylinders, but this lacks anatomical confirmation. The hypothesis of Heiss [28] that a sling of muscle from the trigone functions mechanically as an internal sphincter fails to account for the difference between the state of acute retention and such a state as is presented by Case 3. The control of the external sphincter must certainly be mediated by the sacral segments via the pudic nerves, and an adequate mechanism for its relaxation during micturition is provided by the fifth reflex of Barrington [3]. Our records indicate that contraction of the bladder is the essential stimulus rather than increased pressure which was suggested by Barrington.

Not only did the external sphincter not relax when fluid was introduced into the posterior urethra in Cases 4 and 5, but no change in vesical pressure, as recorded by the second catheter, occurred. Even when some fluid is forced from the bladder past both sphincters by passive pressure upon the abdomen (fig. 19 at *c*) subsequent micturition awaits the development of vesical contraction, which was then identical with that set up by a similar pressure without the passage of fluid. The presence of fluid or tension in the posterior urethra appears therefore to have no appreciable effect on the bladder, and our findings fully confirm those of Frankl-Hochwart and Zuckerkandl [18] in the normal bladder. The activity of reflexes arising in the human urethra and facilitating vesical contraction or urethral relaxation is either extremely feeble or non-existent.

## V.—The Disturbance of Sensation.

The descriptions of the sensations experienced by these patients during distension of the bladder and during micturition were extremely diverse, but could be classified into two groups. A common sensation in all patients, except Case 6, was a sense of fullness of the abdomen when the bladder contained a high volume, and appeared directly referable to a slight respiratory discomfort. It was not related to any particular region by the patient, and appears to be referable only to increase of abdominal capacity and therefore not related directly to the bladder. The other sensations are more particular and will need more consideration. Of the patients with cauda equina lesions, Case 3 presented the most discrete sacral lesion, although the inflammatory nature of his lesion does not allow absolute finality of deduction. He had no sensation from catheterization. During gradual distension he complained of fullness of the abdomen, indefinitely localized, as a volume of 150 c.c. was reached. At a volume of 200 c.c. the sensation developed gradually into painful discomfort which was felt periodically, and its lack of direct relationship to vesical contraction is instanced by its sudden appearance some seconds after a few faint waves had subsided. Filling the bladder from 200 c.c. to 300 c.c. induced pain vaguely referred to the lower abdomen, which became continuous as the volume of 300 c.c. was reached.

Case 2, with clinical evidence of destruction of the cauda equina up to the level of the lower borders of the left fifth and right fourth lumbar segments and recovering function in the lumbar roots, first felt some fullness related to the abdomen at a volume of 335 c.c. An unpleasant sensation, referred vaguely to the left groin, commenced at a volume of 450 c.c. and became rapidly painful when filling was carried further. It was distinctly periodic. In the second experiment he complained of this periodic pain at a volume of 370 c.c., and referred it as before to the left groin. By signalling the periods during which it was felt we found that the pain frequently commenced with the onset of a spontaneous wave of vesical pressure and outlasted several subsequent waves. At other times it was more brief than one wave (fig. 10 E). It would disappear often without any corresponding change of pressure. In a third experiment fullness of the abdomen was first complained of at a volume of 275 c.c. There was no sensation with waves of contraction below this volume (fig. 10). The slightly earlier onset of the sensation of distension in the last experiment might possibly be identified with some recovery of hypogastric innervation. The fullness of the abdomen carried with it no desire to micturate. The unpleasant or painful sensation was also not comparable with normal desire to micturate, for each phase was of extremely sudden onset and intensely unpleasant and was a desire to micturate only in that he would feel a most powerful desire to strain with his abdomen and thus rid himself of it.

Case 1 complained of a slight momentary unpleasant sensation referred to the penis during the first of spontaneous waves of vesical pressure which appeared at a volume of 100 c.c. and again at 150 c.c. (fig. 8). At 160 c.c. he felt a "pumping," throbbing sensation in the upper parts of both thighs, of sudden onset, preceding an outburst of waves of vesical contraction (fig. 8 E). This was repeated with more unpleasant tingling referred to the penis, as further spontaneous waves appeared (fig. 8 F), and became more prolonged as the series of waves lengthened (fig. 9 A). During a later filling a sensation of discomfort referred to the penis, which was completely insensitive, and the thighs, was associated with a sudden momentary desire to pass water, which was extremely unpleasant. This was renewed during a rapid refilling from 100 c.c. to 150 c.c. (fig. 9 B). He once had a sensation of desire to pass flatus and a large rectal contraction was recorded after about six seconds. A similar occurrence is seen in fig. 8 B. This patient also was not conscious of catheterization.

Both Case 1 and Case 2 at first stated that they possessed a sensation of desire to micturate, but close questioning elicited that this sensation was unpleasant or even painful and its rapid development induced them to strain voluntarily. Case 2 stated that he could postpone micturition, but this on close questioning was found to mean that he could tolerate the sensation longer before making a strain to commence micturition. In all three cases a sense of "fullness of the abdomen" formed a very definite part of the sensation during an experiment, but it was probably owing to the binder which was necessary to record abdominal movement.

The three cases with spinal transection experienced no sensation of micturition, with the exception that once in Case 5 some general abdominal fullness was complained of at a vesical volume of 200 c.c. When the binder for the abdominal balloon was readjusted he had no further sensation from distension up to over 300 c.c. During one experiment the occurrence of a large isolated wave of contraction on the recto-colonic balloon was preceded by a sensation of some "slight feeling" in the left lateral abdomen.

The lowest cutaneous sensation in Case 4 was from the right tenth dorsal segment and the left eleventh dorsal segment, and in Case 6 the third dorsal segment. In Case 5 all sensation was absent below the right first lumbar segment and tenth dorsal segment on the left side (fig. 26). Case 4 therefore should possess integrity of that portion of the hypogastric innervation of the bladder which is derived from the right eleventh dorsal segment, and Case 5 from all the hypogastric outflow on the right side. Dr. Carmichael informs us that the right lower limb in Case 5 sweated when the room temperature was raised and this is evidence that the hypogastric (sympathetic) innervation was not impaired on that side. There was no sweating on the left side.

Not only, therefore, may an intact hypogastric nerve give no sensation from the bladder, but the only points in common between the sensations perceived by Cases 1, 2 and 3, and that of normal desire for micturition and of distension, is association with powerful distension and vesical contractions. Their threshold is lower than for sensation in the normal bladder [15]. We agree with earlier writers [32, 2, 18] that normal sensation of the desire to micturate ("Harndrang") is not a function of sensory fibres conveyed by the hypogastric nerves.

The sensations in our cases referable to the hypogastric nerves are certainly provoked by vesical contraction, as Genouville [19] noted of vesical sensation in general. We have found [15] that vesical sensation in the normal bladder may arise without vesical contraction though intensified by such contraction.

## VI.—THE RELATIONSHIP BETWEEN AUTOMATIC AND REFLEX VESICAL FUNCTION.

### (1) *Automatic Micturition resulting from Lesions of the Cauda Equina.*

We have described above the spontaneous automatic micturition we have found following lesion of the sacral roots of the cauda equina. Though our cases are few and the lesions unverified, the clinical states closely adhere to those described by other writers following lesions limited to the conus medullaris and verified at autopsy [41, 2]. This automatism may be identified with that observed in animals after destruction of the lumbo-sacral segments of the spinal cord [22, 41] or degenerative section of the nerves to the vesical plexus [14, 16].

The presence of the hypogastric innervation in connection with the intact portion of the spinal cord lends no voluntary control to vesical function, and, indeed, apart from often conveying sensory fibres it appears to be negligible as a functional entity both in animals and man. That automatic micturition is in any way mediated by it is unlikely, for in animals Elliott [16] and Dennig [14] found complete section of both hypogastric nerves neither to affect the appearance of the condition nor to cause change when the condition had developed. The excisions of spinal cord by Goltz and Ewald [22] and Müller [41] included the segments of origin of these nerves.

In each of our cases of cauda equina lesion the detrusor musculature possesses rhythmical activity even where automatic micturition is limited only to dribbling, as in Case 3. Increase of tension is the adequate stimulus for the appearance of this contractility. It is perhaps conceivable that spontaneous waves appear in continuous series which are merely thrown into prominence by increasing tension on the muscle fibre, but we have also demonstrated that the bladder reacts to sudden increase of tension by a secondary wave of contraction. Such stimulation of vesical contraction appears necessarily to imply a capacity of the muscle fibre to respond to stretch. While a purely local muscular effect for this phasic stretch reaction may not be completely denied, the regular waves of contraction during distension suggest a co-ordination of the contractile process in each fibre taking part. Such synchronizing of spontaneous contractile waves in the whole organ necessitates nervous correlation of some kind. The same conclusion was reached by Elliott [16].

Regular waves of contraction are observable in the completely excised bladder when sufficient tension is imposed (Sherrington [47], Stewart [58]), but these are abolished by careful dissection of the minute mural ganglia (Elliott [16]). The presence of such waves is, however, insufficient alone to secure micturition, for they were observed by Sherrington [47] not to be affected immediately following section of the thoracic spinal cord in the monkey, when the process of micturition is profoundly shocked, and Barrington has shown [5] that in the cat there is no resistance to distension at this time.

Case 3, in whom discrete automatic micturitions did not develop differed from Cases 1 and 2 in that no wave compounds occurred. Though discharge through the sphincters occurred with some small waves in Cases 1 and 2 (e.g., in figs. 16 and 18), the waves are here larger and of longer duration than the unit small wave evoked by sudden distension. There is some evidence, therefore, that for micturition to occur not only must the spontaneous "beating" of the discharge of the vesical plexus embrace sufficient vesical muscle, i.e., involve approximately the whole detrusor, but also that two or more such waves must sum their effect by close approximation (temporal summation). The relaxation of the sphincter appears in records in simple inverse relationship with the contractile activity of the detrusor, so that as spontaneous waves become larger and longer there is greater and more prolonged relaxation of the internal sphincter. The fusions of large waves of vesical contraction into larger complexes is apparent in such records as fig. 18 A. Periodic automatic micturition is conditioned by the capacity of the spontaneous rhythm evoked by stretch of the detrusor to accelerate sufficiently to convert the muscular contraction into a periodic "motor tetanus." This process necessarily implies a correlation of the spontaneous "beating" of the neurones of the vesical plexus, and this in turn requires correlating neurones which dominate large numbers, if not all, of the scattered ganglia. The exact correspondence, the timing of these changes and the periodic relaxations of the sphincter are further strong evidence that extensive nervous correlation is active. There are, unfortunately, no available histological data on the existence of such correlating neurones in these ganglia, the complexity of which has defied histological analysis.

When the spontaneous waves are still single, as in Case 3, the corresponding relaxation of the sphincter is reflected in a more continuous laxity, and consequent dribbling, which accompanies the tonic, more regularly maintained, resistance to the higher grades of distension. Periodicity is a more correlated development of this low-grade automatic micturition.

The full explanation of the stimulation of contraction by increase of tension awaits closer experimental investigation. To call it "reflex" appears premature, for if neither the pelvic nor the hypogastric nerves are essential for its performance there is no known remaining afferent neurone related to that collection of small ganglia which forms the vesical plexus. That the mechanism is essentially neural is certain from its affection by spinal shock. It may be recalled that Langley [35, 36] omitted the enteric plexuses from his conception of the sympathetic system as a purely efferent system and allowed in them a measure of true autonomy. Our findings entirely support the contention of Müller [41] that the vesical plexus also possesses a certain degree of autonomy. Although in our cases the hypogastric outflow was intact, the corresponding spontaneous micturition in dogs and cats with degenerative section of all nerves to the bladder renders insufficient any mechanism based upon axon reflexes in the inferior mesenteric ganglia or vesical plexus, and requires the presence of afferent neurones with cell body situated in the peripheral plexus, and there completing "reflex" circuits.

The smallness of the bladder in some cases is of especial interest and is apparently a constant accompaniment of such lesions in animals (Goltz and Ewald [22] and others), and is accompanied by great thickness and hypertrophy of the vesical wall, described in the human bladder by Lhermitte [39]. In Cases 1 and 3 there is evidence that the bladder will not tolerate much larger volumes than 300 c.c. and the steep curve of emptying, which is a fairly reliable index of the purely elastic reaction of the bladder without tonic contraction, reveals that small volume is related to structural change in the detrusor (figs. 1, 2 and 4). It appears likely that it is the result of a mechanical effect such as obtains for contracture in skeletal muscle. In the normal bladder involuntary reaction to increasing volume is continually subject to procrastination; the average vesical volume is more ample [15]. The fully developed automatic bladder of cauda equina lesions is never subjected to wide distension and the detrusor undergoes contracture to permanent smallness. The condition has been observed in the bladder of the cat after nerve section (16) and also after spinal transection [3].

### (2) *Automatic Micturition resulting from Complete Transection of the Spinal Cord.*

When the nervous lesion isolates not only the bladder and vesical plexus but also a portion of spinal cord including the sacral segments, automatic micturition presents some striking additional characteristics both in reaction to distension and to external stimuli. Spontaneous single waves are still present, but are dominated by phases of explosive maximal contraction of compound nature which also shows a tendency to repetition in slow rhythmical series. These large contractions are also stimulated by increasing distension. They show evidence of compounding of smaller waves, and express, when fully developed, a maximal correlation of summation of muscle-fibre contraction. They are in fact tetanic contractions and must result from rapid repetitive discharge of nerve impulses in volleys. They are accompanied by concurrent prolonged and complete relaxations of the internal sphincter. Arguing from the invariable reciprocal relationship between detrusor and internal sphincter, these relaxations of the internal sphincter may be interpreted as the direct inhibitory result of the same discharge which affects the detrusor.

The general resistance to distension is heightened, forming a tonic background and steeply ascending filling curve which adapts readily to imposed volume. This process of heightened tonic resistance is paralleled by a coincident slackness of the internal sphincter, which we would explain as the result of a fixed simple reciprocal relationship between the two, evident in tonic as in phasic contractions.

The addition of segmental spinal pathways to the nervous mechanism of the vesical plexus endows the peripheral mechanism of reaction to distension with pathways for more extensive correlation. The afferent channels provide for greater efficiency of the tension receptors in the detrusor, the motoneurones allow closer collative activity of the neurones of the vesical plexus. The reaction to sudden momentary tension on the vesical wall is much larger than in the bladder following cauda equina lesions, though the latency of response is not materially altered (cf. figs. 14 and 15). One such sudden stretch is, however, in our experiments alone insufficient to provoke a "maximal contraction" which appears to require a summation of active vesical contraction before it occurs. An equivalent summation of the effects of repeated light stretches, or such brief changes of abdominal pressure as are induced by a cough, deep breath or movement of the patient, can excite maximal contractions, but all require a certain amount of previous distension in addition. Volume is only significant when considered in relation to time, owing to the process of adaptation. The stimulus may be expressed as increment of stretch, and is exactly comparable to that underlying the postural reflexes of the limb muscles.

All these effects are, however, present in the bladder of cauda equina lesions. The characteristic feature of the vesical response which denotes the activity of spinal reflexes is the further process of the "maximal contraction," an explosive response which has a certain latency for elicitation and requires the pre-existence of active vesical contraction. The stretch effects related to the vesical plexus summate, but the summation subsides with cessation of stimulus. The phenomenon endowed by reflexly active spinal segments is that at a certain stage of summation active contraction becomes self-stimulating; the explosiveness of the reaction evidences autogenicity. We see in this process the effect of a fresh variety of afferent nerve ending which commences activity at a certain threshold of active contraction. The activity of this afferent system evokes a correlated discharge of the whole efferent mechanism. The discharge includes rectal activity, prominent in Case 5, less prominent in Case 4, and conspicuously rare in Cases 1, 2 and 3. There is, in addition, perineal movement and relaxation of the external sphincter, to complete the co-ordination characteristic of micturition of the spinal animal. Animal experiment provides ample evidence of the power possessed by the afferents in either pelvic nerve to excite reflex discharge through the other pelvic nerve [51].

No precise histological data on the relationship between preganglionic and peripheral neurones in the intricate vesical plexus is available. It may be compared, however, with the superior cervical ganglion where fibre and cell-counts reveal that each preganglionic fibre by repeated subdivision controls many ganglionic neurones [10] and so provides a basis for extensive correlation.

We have not had the opportunity of following the recovery of the reaction to distension from the initial depression of spinal shock, but it is clear from the work of Holmes [29] that, seen in full perspective, the reaction to distension makes a progressive development in parallel with all other spinal reflexes. Both phasic and tonic reactions of the bladder emerge in a gradual manner from the atony of spinal shock.

In its reaction to change of volume, therefore, this type of bladder differs profoundly from the bladder following cauda equina lesions. The difference is both quantitative and qualitative and is readily appreciable in the regularity, large volume and force of discharge which form prominent clinical characteristics of this type of micturition. We fail to find any differentiation between this reaction to distension and that described by Barrington [3] as his "first reflex." We therefore cannot accept his pontine localization of the reflex mechanism concerned since we find the reaction present with isolated spinal segments, even the limited sacral segments as in Case 5.

The bladder innervated by the reflexly active spinal segments exhibits a further outstanding difference from the bladder of cauda equina lesions, namely a continued closure of the external sphincter, interrupted only by relaxations accompanying each summated vesical contraction. When once opened in this way the sphincter is immediately contracted by any flexion reflex. In Cases 4 and 6 brief scratching of the sole of the foot elicits reflex flexion of the ipsilateral limb, a movement which is accompanied by a contraction of the lower abdominal wall and of the perineum. The immediate change of intra-abdominal pressure brought about by these movements is reflected in a concurrent change in vesical pressure well shown in fig. 46 where discharge of fluid was not allowed and the pressure was therefore uncomplicated by cessation of outflow. The brief latency of these initial changes in vesical pressure, less than one-tenth of a second, following the onset of abdominal and perineal movement, and their rapid decline, exclude their origin from vesical contraction. The latency and form of the delayed response both closely resemble that of the response induced by brief increase of tension. We have attempted to exclude the incidental change of abdominal pressure as a cause of the contraction following plantar stimulation. Flexion of the limb and contraction of the abdominal wall and pelvic diaphragm is abrupt and jerky and lasts at least some seconds. Reduction of strength of stimulus does not succeed in abolishing the induced change in intra-abdominal pressure without also losing effect in evoking vesical contraction. Involuntary flexor spasms, or flexion occurring as a result of contact stimuli, are alike provocative of vesical contraction at times, as in fig. 46 *a*, but then are accompanied by a great deal of abdominal and perineal movement. Plantar stimulation at a time when micturition is not occurring and vesical content is small or moderate (fig. 40 *d*) sets up a wave of secondary contraction without micturition. When micturition is occurring plantar stimulation not only evokes abrupt cessation of outflow, but also, when the immediate pressure change of outflow stoppage has passed, may leave a declining vesical pressure and ultimate cessation of micturition, especially if the stimulus be long continued (fig. 42, *e*), though reopening of the external sphincter occurs (figs. 40 *b*, 41 *c*). Early in a large response a brief plantar stimulation does not cause abolition. All these effects may readily be observed in the urinary outflow of such patients without any catheters or recording instruments, and are not alone evoked by stimulation of the sole, but from any part of the area from which reflex flexion can be elicited. It is necessary to conclude, therefore, that a stimulus sufficient to evoke a flexion reflex secures complete inhibition of micturition during the reflex flexion, but has a much weaker after-effect. This sudden cessation of micturition without doubt may be identified with its reflex inhibition in the spinal animal by "strong cutaneous stimuli" [48].

Head and Riddoch [27] described a rise of vesical pressure accompanying the flexion reflex, but it is noteworthy that although this "mass reflex" was present, discharge of urine through the urethra occurred in one instance only. Their patients possessed fully developed automatic micturition which regularly secured complete discharge per urethram. The lack of actual discharge of urine through the sphincter during the "mass reflex" was explained by the early return of tone to the sphincter mechanism, but in all our own cases added contraction of the external sphincter is effectively preventing actual micturition.

The induction of vesical contraction by a flexion reflex would appear to have some explanation as an indirect effect of the changes of intra-abdominal pressure necessarily also induced. The changes of abdominal pressure are jerky and multiple after even a single prick to the sole, allowing summation of multiple pressures on the bladder. The movements are sufficiently powerful to bulge the perineum (fig. 46 *a*, *b* and *c*).

Cases 5 and 6 were of particular interest in relation to the question of the facilitation of micturition by the flexion reflex. In Case 6 the flexion reflex existed in full development, both in area from which it could be elicited, in lowness of threshold, and in powerful motor effect. Whatever part of its afferent area was subjected to stimulation, the detrusor, lacking only in briskness of stretch response, failed to contract (fig. 50). The external sphincter was immediately contracted by these stimuli although the increase of abdominal pressure at times forced it (fig. 51). Stimulation of the glans penis also failed to set up vesical contraction in this patient (fig. 48), though it caused bilateral flexion of the lower limbs and more powerful closure of the sphincter than stimulation elsewhere (fig. 54). The lapse of one stimulus from a series of pricks reveals clearly the purely passive rise of vesical pressure which results (fig. 49). Stimulation of the left side of the glans penis in this patient produced slightly more perineal movement than did pricking the right side, but was also without effect in evoking vesical contraction. The external sphincter showed well the summation of effect of a series of stimuli (figs. 43, 52 and 53). The degree of development of the flexion reflex appears therefore to have no direct relationship to its power of facilitation of micturition.

Case 5, owing to inactivity of the four lower lumbar segments of the spinal cord, though the sacral segments retained reflex activity, had no reflex flexion. The general reaction of this bladder to distension has been described above. Stimulation of the sole of the foot (fig. 44) or of the glans penis (fig. 45) evoked contraction of the external sphincter, and a degree of perineal movement which was much more powerful than the records indicate. There was a small vibration in vesical pressure corresponding to movement of the perineum, but not comparable in degree to that in Case 4. Stimulation of the sole of the foot by single prick was seldom alone successful in eliciting vesical contraction, but repeated stimulation, or a scratch, was followed by a small vesical contraction (fig. 29 D at *c*, and fig. 58 at *a*). The contraction was identical in latency and form with that produced by brief tension (fig. 29 D). The response was larger with stronger stimuli such as a scratch, but was delayed until a certain latent interval after the scratch (figs. 20 and 58). During the development of a response further stimulation arrested further rise of pressure (fig. 20), but did not abolish the response unless the latter were very small. If recent filling had rendered the detrusor sufficiently active the effects of a series of scratches at

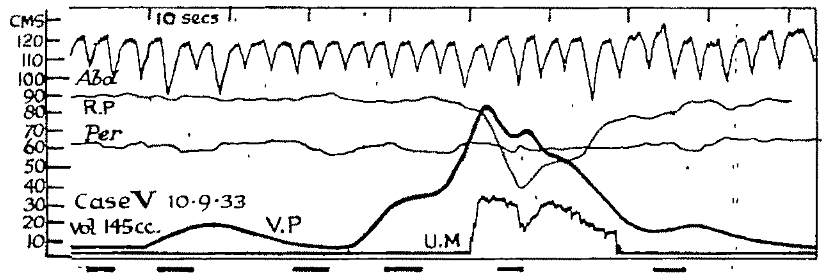

FIG. 20. *Case 5.*—To show the delay in rise of vesical pressure resulting from long slow scratches (duration indicated by horizontal lines at bottom of figure) to the sole of the left foot. The second and fourth scratches appear to impair the development of previous contraction. The catheter had not been completely withdrawn through the external sphincter so that the fifth scratch resulted only in partial monophasic interruption of the micturition which subsequently developed. Reduced to $\frac{1}{2}$.

sufficiently short intervals summated so that a maximal response was eventually elicited by a single prick (fig. 58 *d*).

A single prick applied to the glans penis provoked a delayed vesical contraction (figs. 55 and 57) also identical with a stretch response, and when repeated in series more readily shortened its latency of development (fig. 55) and height of contraction (fig. 57). A rapid series of stimuli was more readily followed by a large maximal vesical contraction than stimuli elsewhere, but it also had some power of inhibiting contraction if strong (fig. 59). Reflex vesical contraction is most readily provoked by weak stimuli, and develops greater tension, when the stimulus is applied to the glans penis, which we regard as the "focus" of this effect just as the outer border of the foot is the "focus" for reflex flexion. Slight inward or outward movement of the catheter is also a strong stimulus of vesical contraction, and light swabbing of the penis or movement of the prepuce (fig. 56) provoked micturition after a brief interval. Lighter movement of the prepuce with care not to disturb the relation of the catheter to urethra did not evoke a response. The delay in appearance of these contractions following these cutaneous stimuli when applied in series is evidence of the dual effect produced by each stimulus. Powerful immediate inhibition suppresses even the excitatory effect of the same stimulus, and only at the end of the series is the excitatory effect declared. Similar "rebound" is frequently observed in limb reflexes. All these stimuli therefore possess some measure of excitatory effect on the detrusor, besides the immediate and more powerful inhibitory effect which accompanies contraction of the external sphincter. We do not think this excitatory effect is, in these circumstances, produced by the small associated perineal movement, for the bladder of this case required a greater degree of applied passive tension to excite contraction than in the more reflexly active case, and changes of abdominal pressure a little greater than those accompanying the reflex response were not successful in eliciting contraction.

Clinical examination of Case 5, however, revealed two features widely differing from the state necessitating the exhibition of the "mass reflex." Although stimulation of the glans penis or of the sole of the foot could bring about facilitation of vesical contraction there was no flexion reflex. Further, it was found that not only stimulation in these areas but also stimulation of the skin in any part corresponding to the innervation of the five sacral segments provoked a motor reflex response quite unlike reflex flexion. Immediately following a single stimulus both thighs slightly abducted, and rotated outwards more strongly, the perineum as a whole was vigorously retracted with contraction of the external anal sphincter, and the great toe on each side was plantar-flexed. The other toes flexed slightly and were approximated. The response was constantly obtained and was increased by prolonged or repetitive stimulation. The motor effect was bilateral from stimulation on either side. The whole area of the sacral dermatomes could be mapped out by it. Stimulation of the lumbar dermatomes on either side, pinching the calf muscles, or eliciting ankle-jerks did not evoke the response. Contraction of the external sphincter of the bladder was as consistently elicited as closure of the external anal sphincter. Occasional slight turgor of the penis found after long intervals of absence of stimulation was abolished by any stimulus provoking micturition or provoking the response above described. No other movement in the paralysed musculature could be elicited. Dorsiflexion of ankle or great toe was not seen. The response appeared as easily elicited from the skin around the anus and from the narrow strip on the posterior aspect of the limb as from the glans penis.

Contraction of the external anal sphincter as a result of a stimulus to the skin around the anus (" anal reflex ") has long been known as an early reflex response to emerge from spinal shock. This " anal reflex " is often the only sign of survival of lower spinal segments following a supraconal lesion. Oppenheim [42] has described how in one such case the anal reflex was elicited by stimulation of the sole of the foot as well as of the skin near the anus, although he does not describe any other motor response. We consider that the reflex response we have described in Case 5 is an extension of the " anal reflex." Its bilaterality, the abduction and external rotation of the thighs and the plantar-flexion of the great toes proclaims its complete independence of the flexion reflex, and the coitus reflex, with their contrary motor effects. We propose to call it " the sacral reflex."

The " sacral reflex " is accompanied by a twofold effect on the bladder. Accompanying the perineal and limb movement the external sphincter contracts and vesical contraction is momentarily inhibited. Following the direct motor effect vesical contraction is stimulated. The reflex facilitation of the detrusor has a focus at the juxta-meatal portion of the glans penis, while the inhibitory effect and contraction of skeletal muscle are as easily provoked from any part of the sacral cutaneous segments. Whatever the nature of the antagonism between these two components of the " sacral reflex " it is clear that the first is a true reflex facilitation of micturition.

The early emergence of the "anal reflex" from spinal shock strongly suggests that, in those cases where a "flexor plantar response" has been obtained in the first days of recovery from an acute transverse lesion of the spinal cord [30], the limb reflex constituting the sacral reflex has appeared. The subsequent substitution of dorsiflexion of the great toe when the sole of the foot is stimulated bespeaks the inhibition of the sacral reflex when the "prepotent" flexion reflex recovers. We have not had an opportunity of observing this transition, but in cases of various partial lesions and one other complete lesion, one of us has observed intermediate stages of domination of the sacral reflex by the flexion reflex.

As a result of investigation of Cases 5 and 6, therefore, we are led to the conclusion that true reflex facilitation of micturition by cutaneous stimuli does in fact exist. Its cutaneous area has a "focus" at the glans penis, and fades through the sacral segments. In Case 4 all stimulation was complicated by the flexion reflex, and we were unable with certainty to deny reflex facilitation from other areas because of the changes in abdominal pressure associated with it. It is certain, however, that inhibition of micturition was more powerful from all these other areas, and only with considerable degrees of existing detrusor excitability, for example, by recent rapid distension, could a flexion reflex evoke subsequent discharge. Stimulation of the glans penis in this patient, besides evoking reflex flexion, was potent in setting up vesical contraction. Attempts to separate the two components of the sacral "reflex" in Case 5 by variation of mode of stimulus, massage of the glans penis (fig. 56), &c., failed to make any such differentiation, though without doubt each has an adequate stimulus. Case 6 exhibited the type of micturition seen after cauda equina lesions, controlled by a reflexly active external sphincter.

Reflex micturition is characterized by explosive vesical contraction which, if our deductions as to origin from autogenetic stimulation be correct, may not be expected to exist long in incomplete form. Cutaneous facilitation in fact evoked such discharge only indirectly, in the same manner as sudden stretch or distension, and we did not find it possible to grade the size of contraction by the intensity or duration of cutaneous stimuli. At one period in one experiment in Case 5, it was found that cutaneous stimuli set up a small combined rectal and vesical disturbance after an interval (fig. 21). This was more readily provoked from the glans penis by one prick, than from the sole of the foot where a series of pricks was necessary. This disturbance did not appear to be graded; for stronger stimulation provoked only a maximal response, but the associated delayed rectal contraction suggests that the afferent stimulation was reaching that efferent system concerned with the combined rectal and vesical maximal contraction so obvious in this patient. We did not find further opportunity to study the phenomenon, and can offer no explanation of the delay in reaction.

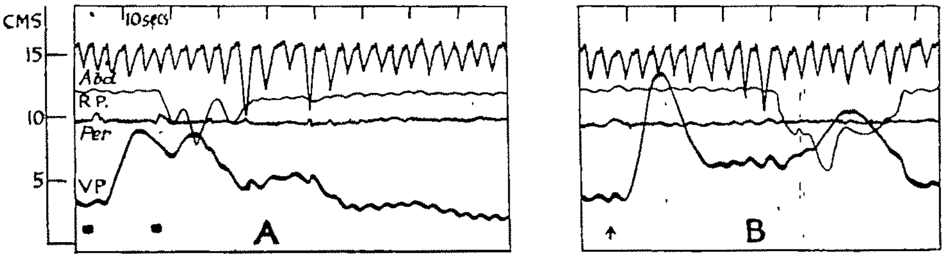

FIG. 21. *Case* 5. August 27, 1938.—Vesical volume constant, 100 c.c. In A the effect of two series of pricks to the outer border of sole of left foot induces vesical and rectal contraction. The duration of each series of pricks is represented accurately by a black square. In B is shown the vesical contraction stimulated by an accurately signalled prick (↑) in the neighbourhood of the urethral meatus. Reduced to ½.

### (3) *Reflex Co-ordination.*

To include the incongruous mixture of brisk, often bilateral, flexion with micturition and widespread sweating as one reflex, the "mass reflex" [27], belies the niceties of reflex co-ordination in every way apparent in the spinal animal. This incongruity in part disappears with our finding that contraction of the external sphincter is reflexly induced by stimulation of the skin surface, as well as some direct inhibition of vesical contractility. The latter is mixed with the directly stimulating effect of abdominal movement. The external sphincter provides an adequate security for the abolition of micturition during reflex flexion and other reflexes. The promotion of evacuation of urine through a catheter by the flexion reflex ("mass reflex") is nullified by contraction of the external sphincter. Patients with reflexly active spinal segments possess an automatic, and usually complete, periodic evacuation of urine which is the result of natural distension of the bladder, although the immediate stimulus was usually some abdominal movement.

We see no justification for the inclusion of micturition in a progressive abolition of "local sign" of reflexes such as that hypothesized for the "mass reflex" [27] and flexion reflex. Indeed, by the well-defined physiological notion of "local sign" (Sherrington [50]), meaning a functional adaptation of reflex movement according to locus of afferent stimulation, the flexion reflex *gains* local sign in its fuller emergence from spinal shock, rather than loses it. When the afferent areas include the thigh there are specific differences in the reflex, according as its outer or inner side is stimulated. The scratch reflex likewise gains local sign with increase in cutaneous area. The flexion reflex from the first affects proximal joints as well as distal joints of the limb; its characteristic physiological feature is withdrawal of the limb as a whole.

The enlargement of the area from which the flexion reflex can be elicited in the process of its emergence from spinal shock has explanation in the progressive recovery of excitability of the motoneurones concerned, without change in the distribution of afferent effects. The reflex fully emerged from spinal shock appears to physiologists the more "normal" reflex, albeit enhanced in after-discharge.

In the normal human being, as in "spinal man," a contraction of the bladder is evoked by a cough, sigh, or other sudden change in abdominal pressure [15]. It here shows the characteristics of the response to momentary change of tension in the automatic bladder, and has the same time relations. This reaction to sudden tension may be regarded as the basal postural response of the organ, as the tendon-jerk of the postural reflex is of striped muscle.

A process of storage of fluid and a process of discharge of fluid may not at first sight appear compatible functions of the same mechanism. Our analysis indicates, however, that the degree of progressive increase of volume which the organ accommodates before discharge occurs is directly related to the intensity of automatic micturition, and is determined by the facility with which stretch of the detrusor can activate the discharge of the neurones provoking contraction. Adaptation to volume in these bladders is seen only as a consequence of cessation or slowing of distension; and reflects the degree of response during the previous distension. The ultimate reaction is inevitable if distension is *progressive*. The only "adaptation" which then occurs is the trough following a maximal fused contraction, and this in turn gives way to another such contraction if distension continues. If the volume is then kept constant, as in figs. 11 and 12, the reaction eventually subsides, only to be renewed with further increase in volume. Each such reaction represents a micturition, which is here only prevented by the occlusion of the catheter. It is thus not comparable to the "plastic tone" of skeletal muscle. In the normal human bladder, on the other hand, adaptation occurs with smaller contractions arising at intervals *during* distension, and is interpreted as the result of inhibition arising from higher nervous levels [15]. The mechanism appears to be identical with that which has been described for rectal function in man [31].

The central locus of co-ordination of vesical activity lies within the small sacral segments of the conus medullaris. We have described the close interaction of automatic micturition, rectal contraction, reflex micturition, and reflex facilitation of micturition, when the functioning spinal segments are restricted to the sacral group. Even in this state micturition does not occur as an isolated nervous discharge but is closely bound in a complex reaction, and for this reason we have refrained from the use of the word "centre." The spinal reflexes use the efferent neurones at their command as a whole, and the activity of one set involves the coincident appropriate adjustment of others.

Micturition in reflexly active spinal man is, by reason of reflex inhibition, frequently incomplete. For that reason it is not uncommon to find considerable volumes of urine remaining in the bladder immediately after a micturition, even in Case 5 where the field for reflex inhibition was limited. Equally frequently Cases 4 and 5 secured complete evacuation of the bladder, and under conditions of experiment micturition was often complete. It has been argued [5] that the small amounts of residual urine often found in the decerebrate and spinal cat are evidence of inco-ordination of micturition. On the contrary, the incompleteness of reflex micturition in the spinal state, and probably also in the decerebrate state, offers evidence of perfected co-ordination and greater harmony between reflexes.

It becomes apparent, therefore, that *moderate* volumes of "residual urine," unless considered in conjunction with the circumstances of the preceding micturition and the details of other micturitions, are without value in estimating the state of micturition. The transition from complete depression of micturition due to spinal shock to recovery of automatic micturition, is by degrees of increasing maximum volume of discharge from decreasing volume of vesical contents. The reverse transition as a result of gradual reflex failure repeats the same stages, of which our Case 6 may be taken to represent an intermediate state. A more important clinical indication of the state of micturition is the volume of the greatest single micturition over a period of twenty-four hours. The volume of residual urine after *the most complete* micturition changes in inverse proportion, but only the considerable volumes of residual urine in states of almost complete failure of vesical function are, when considered alone, of significance.

Close comparison of the records of uninterrupted micturition and of vesical contraction without micturition, in Cases 4 and 5, reveals no element of difference from the records of normal man shown in our previous paper [15]. The salient effect of will in micturition in the normal subject is voluntary suppression, which led us to postulate an hypothesis of voluntary control entirely by inhibition. No feature of spinal micturition appears to us to be incompatible with this conception.

Barrington [4, 5], as a result of a long series of carefully conducted experiments in the cat, concluded that the contraction of the bladder resulting from distension was abolished by interference with a relatively small region of the pons or with descending tracts from that region. Since cats failed to recover from such a lesion he considered this region of the pons an essential link in the reflex reaction to distension (his "first reflex"). We have here demonstrated the full reflex reaction to distension as a purely sacral segmental reaction, and, by analysis, find it only a correlated reflex discharge based on the reaction which can be elicited from the autonomic plexus alone. There is abundant evidence that in spinal man, as in the spinal dog, a reaction to distension occurs as a spinal reflex. The experiments of Barrington, however, localize with great accuracy the region and connections whose injury is responsible for a depression of micturition immediately succeeding pontine or lower section. It is indeed remarkable that this region is identical in level with that responsible for "spinal shock," and we would emphasize the exact parallel which exists between the limb reflexes and the "reflex" reaction to vesical distension. The frequency of micturition of the decerebrate animal thus derives, in our view, explanation as an enhanced spinal reflex, and reflects that enhancement of the stretch reflexes of which decerebrate rigidity is the most obvious outward sign.

## VII.—RECONSTRUCTION OF THE DEVELOPMENT OF AUTOMATIC MICTURITION.

The sudden onset of a complete lesion of the spinal cord at any level has long been known to be followed by a period of retention of urine. The detrusor musculature lies atonic and the internal sphincter, in inevitable reciprocal relationship, falls into uninterrupted closure. The external sphincter, in common with other voluntary musculature, lies flaccid and toneless. We may reconstruct from our own findings and from the deeper perspective of the findings of Holmes [29] the following outline of subsequent events concerning micturition.

As the initial shock passes the detrusor awakens to greater development of reaction to stretch and rhythmical contractions become more prominent. The re-establishment of micturition awaits sufficient degree of contractile activity, especially of rhythmical activity of the detrusor. At first a degree of intensity of vesical contraction sufficient to reflect only some laxity of the internal sphincter is attained and micturition by passive increase of vesical pressure becomes possible. In more ample development the same local mechanism gains, by periodic fusion of waves of contraction, a deeper and more prolonged reciprocal relaxation of the internal sphincter so that periodic discharge commences. Automatic micturition of low grade is thus established as a function of the bladder and related pelvic plexus. Unrestrained by any other activity it functions frequently, although often anticipated by passive increase of vesical pressure by straining and other abdominal movement. As automatic micturition gains in efficiency so the vesical volume lessens and the detrusor may even show contracture.

Further co-ordination of the contractions of the detrusor requires the assistance of correlation from the sacral segments of the spinal cord (true reflex micturition) which brings also an association of rectal and vesical activity. The integrity of these sacral segments also allows the recovery of function in the striped musculature of the sacral segments, including the vesical sphincter. This sphincter regains a postural tonic contraction even when these other muscles lie flaccid and the summated detrusor contractions in reflex manner secure its relaxation for discharge. The external sphincter provides the means for rapid co-ordination of micturition with other spinal reflexes.

True reflex facilitation of micturition is confined to the effects of stimulation of the sacral cutaneous segments, and even here is in greater part negatived by the further development of the omnipotent, "prepotent" flexion reflex. In spinal man, as in the spinal animal, manifold under-currents of reflex activity are hidden beneath any purposive movement, for which inborn reflex co-ordination secures perfected outward expression.

The pelvic nerve and the pudic nerve together form the efferent pathway for reflex micturition. The hypogastric innervation is without significance and may be disregarded in this connection, and disturbance of sensation referable to it gives equivocal indication of the location of disturbance. Occasionally fibres of long extramedullary course conveying sensation from the bladder allow undoubted vesical sensation, notably the pain of extreme distension, to circumvent a lesion even in the lower dorsal region. Our cases are not consistent in this respect. The distribution of afferent fibres to visceral organs in common with sympathetic fibres allows wide segmental divergence and variability. Normal sensation of desire for micturition ("Harndrang") is regularly abolished by limited sacral lesions, though some sensation, usually unpleasant or painful, of imminent micturition may be retained.

Stretch of the detrusor is the adequate stimulus for vesical contraction and its effect may be sampled by a brief passive pressure. With the development of a simple automatic reaction after lesions of the cauda equina, there is a small response to brief pressure. With the more active bladder of the isolated segments of the spinal cord the reaction occurs to lighter pressures and is more brisk, while heavier pressures may impair the reaction. By the criterion of heavy pressure slowly applied on the lower abdomen the vesical contents are more easily expressible after lesions of the cauda equina. The reaction of the bladder of the reflexly active spinal segments to brief transient pressures is such that movements of the patient, coughs or deep breaths, more frequently commence discharge than uninterrupted filling of the bladder which is alone effective practically only during sleep.

## SUMMARY OF CONCLUSIONS.

(1) The registration of the pressure of the contents of the human bladder during its distension reveals the occurrence of contraction of the detrusor elicited by stretch of that musculature. The reaction is elicited only by increment of stretch, and at continuous stretch or by decrease of stretch, the reaction progressively declines. The volume of the contents of the bladder expresses the stimulus for this reaction only when related to the proportion most recently added.

(2) Increase of passive pressure on the bladder likewise evokes contraction of the detrusor. By means of brief transient passive pressures small twitch-like contractions of regular duration may be elicited, and these are related to the general reaction to continued stretch. Passive pressure on the bladder derives greater effect if alternating in intensity, by reason of the response to rapid acceleration of pressure.

(3) This reaction of the detrusor to stretch recovers progressively from the shock of sudden complete transverse lesions of the spinal cord or cauda equina. The mechanism of the reaction is related only to the vesical plexus and detrusor, and a peripheral reaction of reflex character must be postulated to account for it.

(4) This reaction of the bladder to stretch is found in an enhanced form when reflexly active spinal segments make full recovery from

spinal shock. The mechanism is probably still wholly related to the vesical plexus.

(5) The sacral spinal segments may set up discharges of the whole detrusor mechanism by a reflex for which the adequate stimulus appears to be a certain degree of active reaction to distension. This is true reflex micturition and its discharge may affect the rectal division of the pelvic plexus as well as the vesical plexus. The hypogastric nerves play no part in the efferent reflex mechanism, or in voluntary control.

(6) The efferent neurones which serve reflex micturition are subject to excitation by cutaneous stimuli from the sacral segments with a focus of effect at the urethral meatus. The effect is smaller from the first and second sacral segments, and it is doubtful if it may be obtained from the lumbar segments. This is reflex facilitation of micturition.

(7) From the sacral segments a reflex response, the "sacral reflex," which includes the anal reflex, exerts a transient inhibition upon the discharge of reflex micturition. The flexion reflex exerts a stronger and more lasting inhibition of reflex micturition. Neither appears to inhibit the activity of the peripheral response to stretch, so that the abdominal movement with the flexion reflex tends by its stimulating effect to oppose the later stage of inhibition of reflex micturition. With the effects of the "sacral reflex" merges reflex facilitation of micturition.

(8) The internal sphincter reflects a degree of contraction reciprocal to that of the detrusor at the time, and is not under separate control.

(9) The external sphincter is reflexly active where the sacral segments survive, and maintains a tonic contraction which is relaxed reflexly by a certain degree of active vesical contraction. By its contraction in the course of all reflexes other than reflex micturition it secures co-ordination between micturition and these other reflexes whatever the state of activity of the detrusor. The recovery of tone in this sphincter appears responsible for the onset of late resistance to catheterization in these patients.

(10) The reactions of the bladder mediated by the vesical plexus and sacral segments of the spinal cord differ from those of the normal bladder only in lack of appropriate restraint.

(11) We recognize three fundamental states of disturbance of micturition by complete spinal lesions. A depression of function with inactive detrusor and tonic internal sphincter is the transient immediate result of a sudden deprivation of innervation. The development of incontinence during straining movements and later spontaneous inter-

mittent micturition characterizes the isolated survival of the peripheral plexus. A more facile and complete development of automatic micturition, co-ordinated with defæcation and subjected to the interplay of spinal reflexes, reveals the reflex behaviour of the isolated sacral segments of the spinal cord.

## APPENDIX.

### DESCRIPTION OF CASES.

*Case* 1.—*Complete bilateral lesion of 5th lumbar and all sacral roots of the cauda equina.*

G. S., aged 26, admitted January 5, 1933, under the care of Dr. Gordon Holmes.

*History.*—Mining accident, February 9, 1932, with immediate loss of the use of both lower limbs and loss of sensation below the groins. Subsequent retention of urine. Indwelling catheter for nine days, and since then "incontinence" of urine associated with ability to assist urination by straining. He remained unconscious of bowel movements, which he could not control. After four months there was gradual recovery of flexion at the hip-joint and of some extension of the knees.

*Clinical state at time of experiment.*—Some weakness of the lower abdominal wall was revealed by bulging on coughing; flexion, abduction and adduction at hip-joints and extension of knees of moderate power; extension of hips and flexion of knees very weak. No voluntary power in movement of toes or ankles. Fibrillation present in glutei, with some wasting of glutei, vasti and hamstrings on both sides; gross wasting of calf muscles and intrinsic muscles of feet. Reflexes: Lower abdominal reflexes diminished but equal, right knee-jerk present, left absent, both ankle-jerks absent. No plantar response. The anus was patulous.

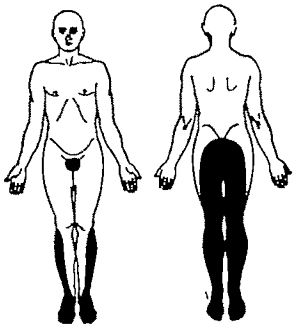

FIG. 22.

Complete loss of sensation to all forms over an area corresponding to the

5th lumbar and all more caudal segments (fig. 22). X-ray of spine revealed fracture dislocation of body of 4th lumbar vertebra.

*Micturition.*—No actual knowledge of passage of urine apart from preceding abdominal sensation. He commenced micturition every fifteen minutes by straining down, and would strain until no further evacuation occurred. Micturition did not always result from straining. Urine would pass spontaneously if the straining process were not made sufficiently frequently, and he was unable to prevent its passage. For the duration of one strain the stream was relatively forceful, and ended without dribbling as soon as he ceased straining. He was found to have about an ounce of residual urine. He stated that he had no sensation of distension of the bladder, except abdominal discomfort when his bladder was full. He was conscious of the presence of flatus in the bowel and could succeed in passing it, or a motion, by straining. Experiment January 8, 1933.

*Case 2.—Complete bilateral lesion of fifth lumbar and all sacral roots of the cauda equina, partial lesion of first four lumbar roots.*

F. B., aged 22, admitted to the National Hospital on October 6, 1932, under the care of Dr. James Collier.

*History.*—Six months before admission crushed in a colliery accident with immediate complete paralysis of lower limbs, loss of sensation below the groins, retention of urine, and loss of control of bowels. After catheterization for six weeks involuntary micturition commenced. Some return of sensation over the front of the thighs commenced three weeks after the accident, and five weeks later some recovery of extension of both knees. He had regained no control over evacuation of the bowels.

*Clinical state.*—Weakness of lower abdominal musculature on both sides. All voluntary movements at the hip-joints weak except adduction. Flexion of both knees weak, extension powerful. No voluntary movement at ankles except faint dorsiflexion of the left ankle and inversion of the right ankle. The limbs lay extended with extreme wasting and flaccidity of all muscles, except the adductors of the thighs and extensors of the knees. The abdominal reflexes were present, the right knee-jerk absent, the left sluggish. Both ankle-jerks were absent and there was no response to plantar stimulation. The anal sphincter was patulous. There was diminution of all forms of sensation over the skin corresponding to the 2nd, 3rd and 4th and left 5th lumbar segments. Over the 5th lumbar on the right side and all sacral segmental areas on both sides there was complete loss of all forms of sensation (fig. 23). X-ray of spine shows fracture dislocation of 1st lumbar vertebra.

*Micturition.*—Preceded by the sudden onset of an unpleasant "desire to pass water," accompanied by an intermittent ill-defined sensation in the left groin, which lasted for several seconds and recurred about once a minute, until relieved by micturition. At first evacuation occurred inevitably immediately following the onset of this sensation, but by the time of the first experiment this sensation preceded micturition for three to five minutes, and by the time of the second and third experiments for ten to fifteen minutes, being then accompanied by a sensation of swelling in the lower abdomen. He attempted to assist the passage of urine by straining and the stream started immediately. He was unable to terminate voluntarily the powerful stream which resulted. Such expulsion of urine occurred about once an hour; there was no dribbling. He had no knowledge of ability to pass urine without the presence of the sensation referred to the groin, and there was no sensation of passage of urine apart from relief from the sensation referred to above. He could pass a little urine by straining without previous sensation. At the time of the third experiment he stated he had some slight sensation of the passage of urine (relief from previous sensation) and of the passage of the catheter through the meatus, although no recovery of sensation in the cutaneous areas of fifth lumbar and sacral segments had occurred. Experiments. October 15, November 13 and 27, 1932.

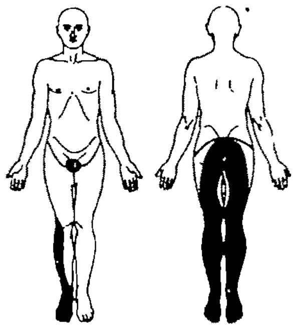

FIG. 23.

*Case 3.—Complete bilateral lesion of the third, fourth and fifth sacral roots, partial lesion of second sacral roots.*

G. G., aged 17, admitted under the care of Dr. Gordon Holmes on July 24, 1933.

*History.*—Having previously been in good health, towards the end of May he commenced to suffer from an ache over the sacrum, most intense in the mornings. Two weeks before admission he awakened with a numbness of the buttocks and perineum, he could not pass urine, and was catheterized at regular intervals from that time onwards. The numbness persisted. After forty-eight hours he commenced to suffer from bouts of burning pain in the backs of the thighs which occurred two or three times a day from that time onwards for two weeks. Three days after the onset of the numbness he first noticed weakness of the lower limbs which was slight and did not interfere with walking. At the time of his admission to hospital eight weeks after the commencement of his illness the cranial nerves, upper limbs and trunk showed no abnormality. There was no defect of motor power of the lower limbs with the exception of some doubtful weakness of plantar flexion, no wasting and no fibrillation. The perineum bulged with respiratory and other abdominal movements. The tendon-jerks were all present and equal in the upper limbs, the abdominal reflexes were present and equal, the knee-jerks were both brisk and equal, the right ankle-jerk was present, the left absent, the plantar responses were flexor. No form of sensation was appreciated over the distribution of the 3rd, 4th and 5th sacral segments (fig. 24), and there was some impairment of all forms of sensation over the area corresponding to the 2nd sacral segment on both sides. Complete inability to pass urine. No sensation from the bladder except severe lower abdominal pain when distension became extreme. No sensation from catheterization. He had no control over the movements of the bowels. His urine was found to be grossly infected and the bladder was from that time washed out regularly. On July 31 examination of the cerebrospinal fluid showed an initial pressure of 60 mm. Jugular compression caused a slow rise and a slow fall. The fluid was clear and colourless and contained one cell per c.mm., total protein 0·2 per cent., globulin strongly positive, Wassermann reaction negative.

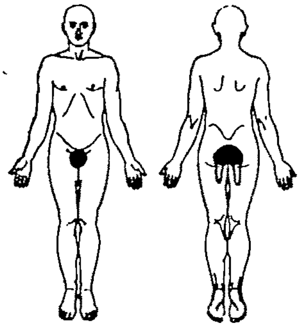

FIG. 24.

Three weeks before the experiment he found that after prolonged straining he could pass some urine. In the next two weeks he found that he could pass urine with a little less straining. He still had no sensation of moderate distension and no sensation of passage of urine, and during this two weeks the only indication of sufficient distension to allow passage with straining was the occurrence of involuntary dribbling which he was unable to prevent by voluntary effort. This dribbling would occur a number of times a day. In the week before the experiment voluntary evacuation of urine occurred much more easily than before, although he still had to bear down to initiate passage. At the same time the amount of involuntary dribbling became much less, though still occurring at intervals during each day. With such dribbling he had an unpleasant feeling of desire to micturate, which also was first felt one week before the time of the experiment.

*Diagnosis.*—Sacral neuritis.

*Clinical state at time of experiment.*—Careful examination could demonstrate no weakness of movement in either lower limb. A remarkable feature was the laxity of the perineum. A slight cough when the patient was in the prone position caused pronounced bulging of the perineum (S. 3, 4). He was unable to withdraw the perineum voluntarily. The glutei were of good bulk and contracted firmly on movement. The left ankle-jerk was still absent. Loss of sensation was still complete over the third, fourth and fifth sacral segments and partially over an area corresponding to second sacral segment. Experiment April 27, 1933.

*Case* 4.—*Complete transverse lesion of the spinal cord at the level of the eleventh and twelfth dorsal segments with impairment of the tenth dorsal segment.*

C. T., aged 35. Admitted to the National Hospital January 17, 1933, under the care of Dr. Adie.

*History.*—Accident September 3, 1931, with immediate loss of power of movement of lower limbs, of sensation below the level of the umbilicus and retention of urine. Commencement of involuntary flexion movements of left knee eight months after the accident and of right knee three to four months later. The upper level of the sensory defect had receded to the groins about eight months after the accident, and from that time there was no further recovery. There was no return of motor function. He had an indwelling catheter, through which his bladder was washed out daily for ten months. With removal of the catheter it was found that the passage of urine occurred spontaneously about once an hour. This occurrence was preceded for a very brief interval by the appearance of a palpable swelling in the mid-hypogastrium. Massage of the lower abdomen could at times cause the appearance of this swelling (contracting bladder) and bring about the occurrence of micturition which it invariably preceded. Spontaneous penile erection occurred frequently and was abolished by micturition. He had no voluntary control over defæcation, but had found that massage of the abdomen in the left iliac region occasionally induced it

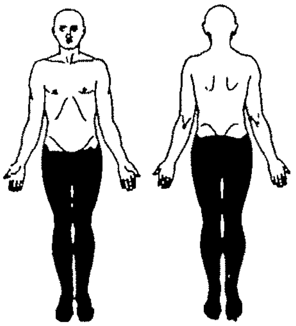

FIG. 25.

*Clinical state.*—Some weakness of muscles of lower abdominal wall. There was no voluntary power in the lower limbs, which lay extended with some increase in tone in extensors of both knees and plantar flexors of the ankles. There were occasional brief momentary spasms of flexion in both lower limbs. Arthritic changes in both knee-joints and both ankle-joints limited movement. Upper abdominal reflexes present, lower absent. Knee and ankle jerks brisk and ankle clonus present on both sides. Extensor plantar response on right side. Flexion of limb but no toe movement on stimulation of the sole of the left foot. There was complete loss of all forms of sensation below the tenth dorsal dermatome on the right side and eleventh on the left (fig. 25). Above this level there was some slight loss of sensation corresponding to the tenth dorsal segment (not shown in fig. 25). A scratch of the skin in any part of the lower limbs, from the first lumbar skin segment downwards, elicited reflex flexion of the limb stimulated. X-ray of spine revealed fracture dislocation of body of the tenth dorsal vertebra. There was a chronic infection of the urine. Micturition was periodic, forceful, abrupt in onset and cessation, and usually secured complete evacuation. It could be interrupted, often for long intervals, by reflex flexion. Experiment February 18, 1933.

*Case 5.—Transverse lesion of the spinal cord, causing total destruction of second, third, fourth and fifth lumbar segments and partial affection of eleventh and twelfth dorsal and first lumbar segments.*

D. McK., aged 28. Admitted April 20, 1933, under the care of Dr. Carmichael.

*History.*—Fourteen months before admission fell 30 ft. at sea with immediate complete loss of movement of lower limbs. According to the patient's statement he was not aware of any loss of sensation. He was unable to receive medical attention for three days. He stated that he had been incontinent of urine from within the first few days after his accident onwards. There was no sensation of distension, nor any control over urination or defæcation. He developed a sacral bed-sore. After some weeks the level of loss of sensation receded. Five months before admission small-involuntary movements of the right lower limb commenced to occur, and within a short time involved the left lower limb as well.

*Clinical state.*—Weakness of the abdominal muscles below the umbilicus on both sides. There was no power of voluntary movement in the lower limbs, which lay extended with reduced tone in all muscle groups. The muscles of both lower limbs were wasted. There was a faint upper abdominal reflex on both sides, the middle and lower were absent. Neither knee-jerk could be elicited. Both ankle-jerks were present. There was no ankle-clonus. No reflex flexion or dorsiflexion of the great toes or of knee- or hip-joints could be obtained from any part of the limbs. A brisk anal reflex could be evoked from both sides, accompanied by some external rotation of the thighs and slight plantar flexion of the great toes. This reflex could be obtained from the segmental areas of the sacral segments, and is discussed in the text. There was loss of all sensation below a level corresponding to the lower limit of the tenth dorsal segment on the left side and of the first lumbar segment on the right side (fig. 26). X-ray revealed fracture and partial collapse of the body of the eleventh thoracic vertebra. Lumbar puncture gave evidence of complete spinal block. Wassermann reaction of fluid was positive, but no evidence of inflammatory change.

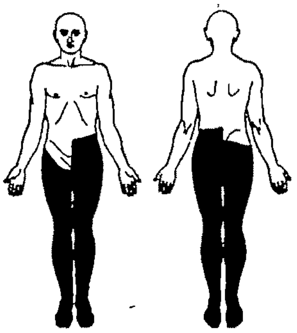

FIG. 26.

*Micturition.*—No sensation of distension of bladder. Spontaneous abrupt evacuation at varying intervals up to two hours unaccompanied by sensation. Stream forceful without dribbling. He could commence micturition by straining down for about a minute, and if there had been an interval since the last evacuation almost any abdominal movement would be followed by the occurrence of micturition. Often evacuation was complete, but it was interrupted by stimulation of the sole of the foot and then seldom recurred within many minutes. Experiments May 27, August 27, September 2 and 10, 1933.

*Case 6.—Complete transverse lesion of the third dorsal segment of the spinal cord.*

H. S., aged 20. Admitted September 25, 1933, under the care of Dr. Gordon Holmes.

*History.*—On June 20, 1933, the patient's arms were drawn between heavy rollers, the forcible extension of his neck eventually stopping the machine. He sustained multiple fractures of his upper limbs, and on recovering consciousness thirty-six hours after the accident, he retained no sensation and no voluntary movement of the trunk or lower limbs. He was unable to pass urine, and until the date of admission to the National Hospital urine was passed through an indwelling catheter. He was incontinent of fæces and no recovery of motor or sensory functions occurred.

On admission he was extremely emaciated, the left pupil was smaller than the right and there was ptosis of the left upper eyelid. There was general wasting of the muscles of the arms, most marked in the intrinsic muscles of the left hand, but no complete loss of power. All muscles except the diaphragm below the second intercostal muscles were completely paralysed. Both lower limbs lay extended, and spasms of involuntary flexion occurred from time to time, more often in the right leg than in the left.

The deep arm reflexes were all present, but more brisk on the right side. Transient, easily fatigued localized abdominal reflexes could be obtained. The knee and ankle jerks were brisk on the right, less active on the left. The hamstring jerks were very active. No ankle-clonus could be elicited. Plantar stimulation produced a brisk dorsiflexion of the great toe on the right side, a less brisk dorsiflexion on the left, as well as brisk flexion at knee and hip. Loss of sensation complete below D1 (fig. 27).

Stimulation of any part of either lower limb evoked reflex flexion at the hip, knee and ankle joints, brisker on the right side than on the left, occasionally with some flexion of the opposite limb. There was no obvious abdominal or perineal movement. The reflex could be obtained from the lower abdominal wall on both sides and from the glans penis; it required stronger stimulation over the glans penis than elsewhere and over the left side than over the right. The perineum appeared indurated, probably as the result of the indwelling catheter, and no local response to scratching of the perineal skin was observed.

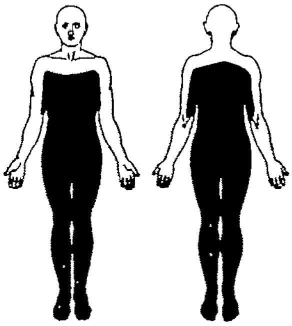

FIG. 27.

The musculature of the lower limbs was loose and atonic, apart from some heightened resistance of the flexors which persisted for a short interval after involuntary or induced reflex flexion.

The urine was grossly infected and was discharged in small dribbling quantities at irregular intervals. He was catheterized twice daily for purposes of vesical lavage and the vesical contents were found to vary from 84 to 280 c.c. Fluid run into the bladder was returned with moderate force when a volume of 280 c.c. was reached. Spontaneous defæcation occurred at intervals. He had no sensation of vesical distension, micturition or defæcation. There was no spontaneous sweating below the level of the lesion, but if covered by too many blankets profuse sweating occurred over the upper limbs, neck and head, and especially over the left side of the face.

On admission he was suffering from a profound general toxæmia with a large sacral bedsore and from his condition he died on October 13, 1933. At autopsy the spinal cord was found to be completely softened in the region of the third dorsal segment. The spine of the second cervical vertebra was unduly prominent but no fracture was detected.

Experiment September 30, 1933.

We wish to express our indebtedness to Dr. Gordon Holmes for his constant interest and encouragement, and to the various members of the honorary staff of the National Hospital who have so kindly allowed us to investigate their patients.

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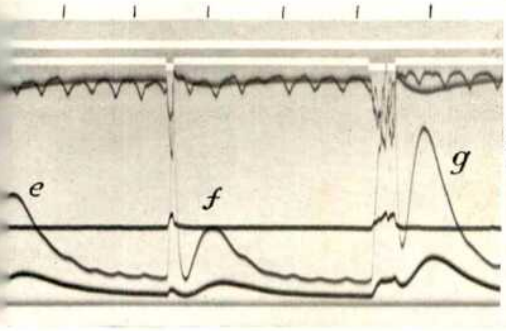
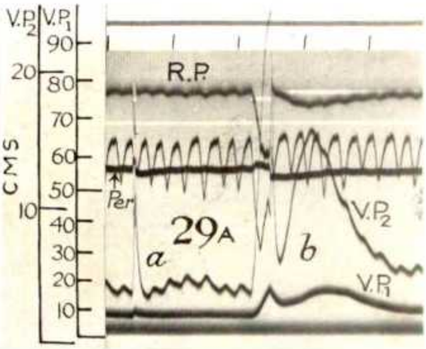
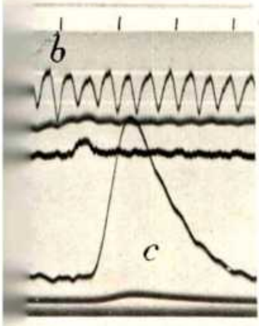
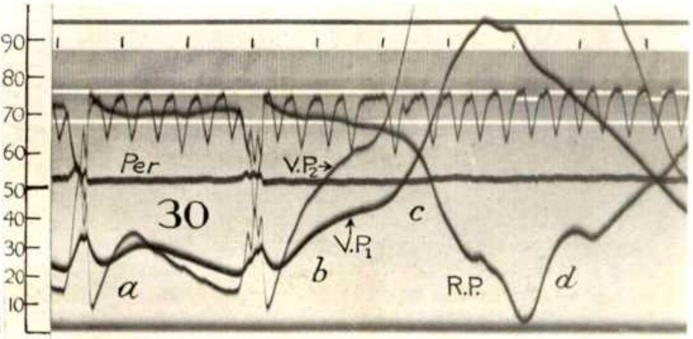

e
f
g


V.P2
V.P1
20
10
CMS
90
80
70
60
50
40
30
20
10
R.P.
Per
29A
a
b
V.P2
V.P1


b
c


90
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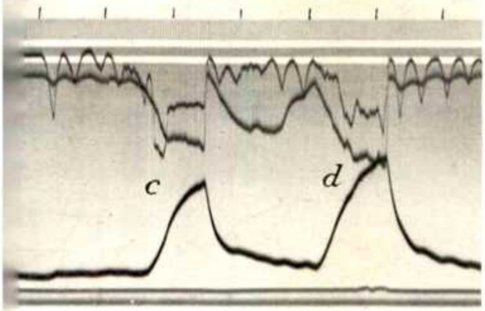
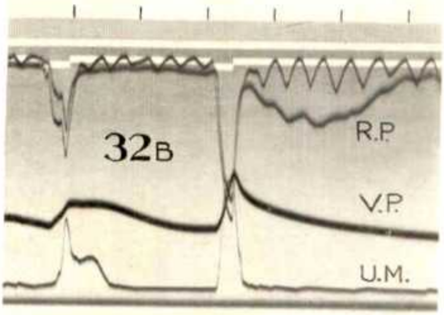
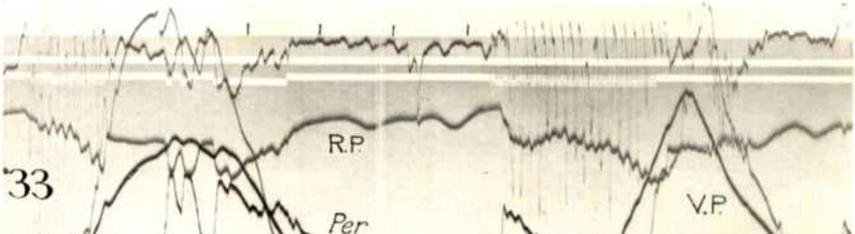
c
R.P.
d


c
d


32B
R.P.
V.P.
U.M.


33
R.P.
Per
V.P.
U.M.

## PLATE XV.

As in the figures in the text, the vesical pressure is indicated by the manometer V.P.1 and also, when the bladder is not being filled, by the manometer V.P.2. Increase in rectal pressure (R.P.) produced downward excursion in the record as does also outward movement of the abdominal wall (Abd). Outward movement of the perineum is indicated by upward movement of the corresponding manometer (Per.). In records of discharges through the sphincters one manometer (U.M.) records the occurrence and pressure of discharge. Time marked in one-fifth seconds at top of record. For convenience of reader intervals of ten seconds have been marked upon each record.

FIG. 28. *Case* 4.—Constant vesical volume 100 c.c., showing effect of passive pressures of varying duration upon lower abdomen.

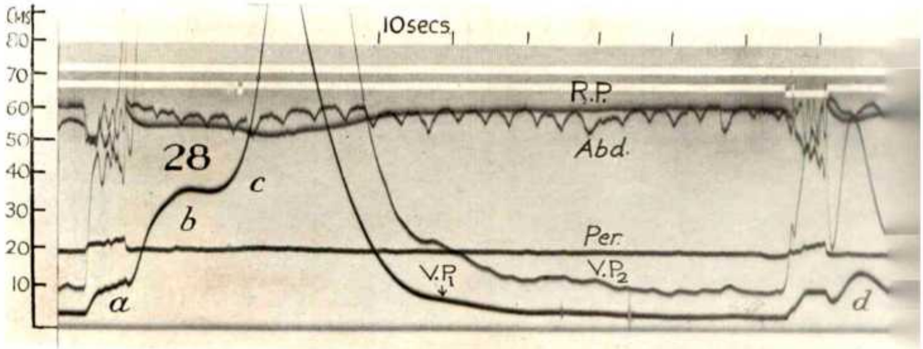
FIG. 29. A, B and C, *Case* 5, May 27, 1933. Fig. 29 D from *Case* 5, August 27, 1933. To show effects of passive pressure of varying duration. At *b* in 29 D a scratch to sole of left foot induces the contraction *c*.

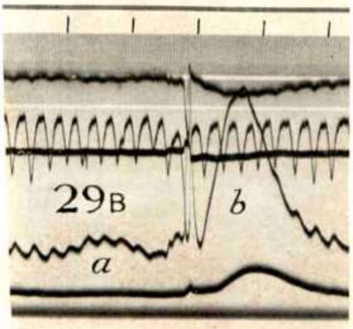
FIG. 30. *Case* 5.—May 27, 1933. Volume 215 c.c. To show the effect of two pressures on the abdomen, the second of which is a little more irregular than the first.

FIG. 31. *Case* 3.—To show the effects of voluntary straining in provoking discharge through the sphincter which outlasts the strain.

FIG. 32. *Case* 1.—Volume 200 c.c. In A the second of two voluntary strains *a* and *b* secures some momentary discharge through the sphincter, and the second of two passive pressures on the bladder *c* and *d* secures the passage of two drops of fluid. In B and C brief strains secure discharge while D and E show the effect of prolonged straining.

FIG. 33. *Case* 4.—Volume approximately 200 c.c. The urethral manometer (U.M.) is just out of communication with the bladder but is found to show the early commencement of discharge during the vesical contraction which is stimulated by abdominal massage. In the first of the two responses, which are directly continuous, two brief and one prolonged scratch to the sole of the foot induced flexion reflexes which affect discharge through the sphincter only by variations of intra-abdominal pressure. Scale of vesical pressure as in fig. 28.


CMS
80
70
60
50
40
30
20
10
10secs
R.P.
Abd.
28
c
b
Per.
V.P1
V.P2
a
d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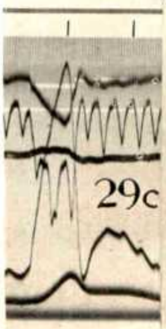
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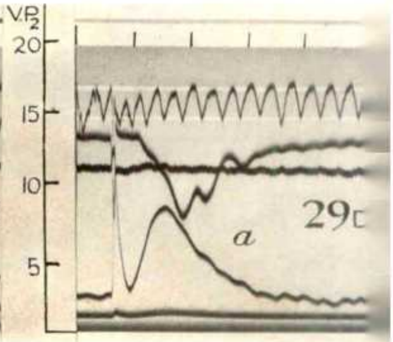
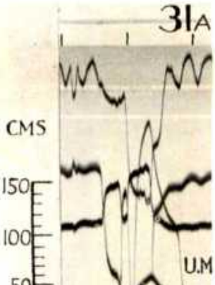
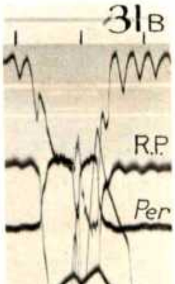
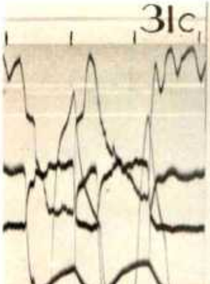
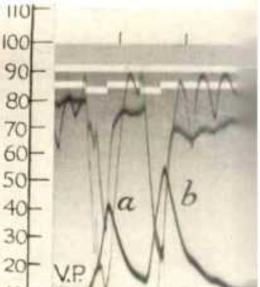
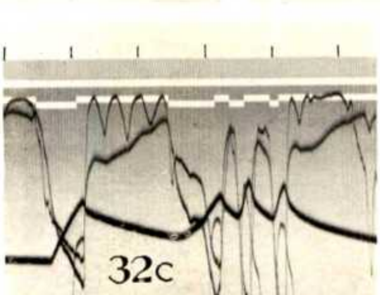

V.P2
20
15
10
5
a
29D

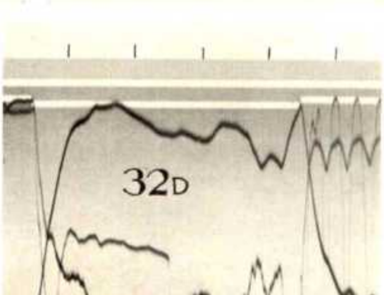

31A
CMS
150
100
50
U.M


31B
R.P.
Per


31C


110
100
90
80
70
60
50
40
30
20
10
a
b
V.P.
U.M.


32C


32D

3

## PLATE XVI.

FIG. 34. *Case* 5.—September 10, 1933. Urethral catheter just out of communi- ion with bladder. The duration of three long scratches along the outer border of e left foot is shown by three successive movements of the uppermost white signal e. A micturition of 40 c.c. occurs. Initial volume 125 c.c.

FIG. 35. *Case* 6.—Urethral catheter just out of communication with bladder. ibbling discharge through internal sphincter with wave of vesical contraction. No scharge in last ten seconds (resting level of manometer U.M.).

FIG. 36. *Case* 6.—Urethral catheter just out of communication with bladder. ief passive pressure on abdominal wall provokes a more lasting discharge.

FIG. 37. *Case* 6.—Urethral catheter withdrawn well beyond region of external hincter. Spontaneous jerky discharge during filling of bladder. Vesical pressure ot shown owing to inflow through ureteric catheter.

FIG. 38. *Case* 4.—Urethral catheter withdrawn just distal to region of external hincter. Micturition evoked by massage. The resulting discharge is of sudden nset with jerky interruptions at *a*, *b* and *c*. Volume approximately 200 c.c. 25 c.c. scharged. The scale of vesical pressure applies also to figs. 39, 40, 41, 42 and 46.

FIG. 39. *Case* 4.—Spontaneous micturition evoked by rapid filling to 120 c.c., and s in progress at beginning of figure. Resting level of urethral manometer indicated y its position in the last three seconds of the record. At *d* and *e* the durations of vo scratches to the sole of one foot are indicated by the breaks in the lower white ne. Fluctuation in other parts of the record, and the rapid changes in discharge at , *b*, *c*, *f*, *g* and *h*, arise spontaneously.

FIG. 40. *Case* 4.—Urethral catheter beyond external sphincter. Spontaneous ischarge. To show effect of scratching sole of foot at *a*, *b*, *c* and *d*. Volume 160 c.c. 0 c.c. discharged.

FIG. 41. *Case* 4.—Initial volume 120 c.c. Micturition initiated by massage. Four scratches to sole of foot indicated by duration of fall of signal line above *a*, *b*, and *d*.

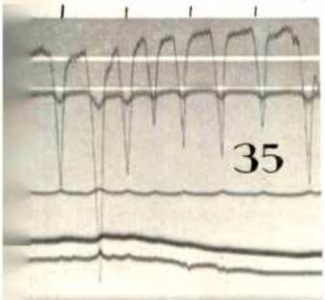
FIG. 42. *Case* 4.—The same stimulation as in fig. 41 repeated during spontaneous micturition. Vesical volume 160 c.c.

FIG. 43. *Case* 6.—Spontaneous discharge during filling of bladder in progress at commencement of figure. A scratch to sole of left foot at break in upper signal line evokes immediate complete cessation of micturition which is recovered from at *a*. A single prick to the sole of the right foot at *b*, and a rapid series of four single pricks at *c* also evoke complete cessation of discharge. The signal is here actuated by an electrical contact made by the movement of the pin.

FIG. 44. *Case* 5.—September 10, 1933. Micturition evoked by massage. A scratch along the sole of the left foot at fall of signal at *a*. Initial volume 200 c.c. Total discharge 50 c c. Scale of vesical tension identical with that in fig. 34.

FIG. 45. *Case* 5.—September 10, 1933. Two series of four pricks each to the glans penis are made at *a* and at *b*, with single pricks at *c*, *d* and *e*. Initial volume 155 c.c., 50 c.c. discharged. Tension scale as in figs. 34 and 44.

FIG. 46. *Case* 4.—Volume 100 c.c. At *a* a spasm of flexion was evoked by the removal of a sock from the left foot. At *b* and *c* the duration of fall in the white signal line indicates the duration of a scratch to the sole of the left foot. Both catheters within the bladder and record vesical pressure. Tension scale as in fig. 38.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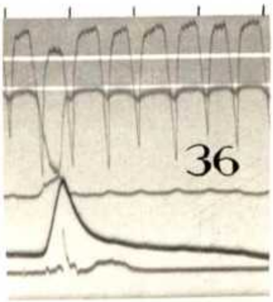
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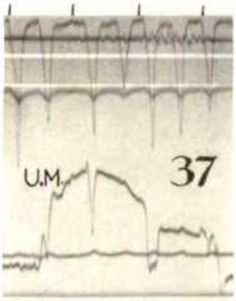
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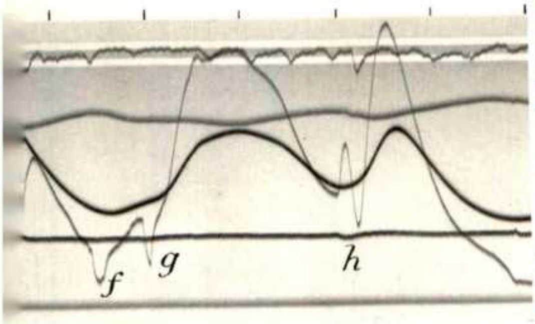

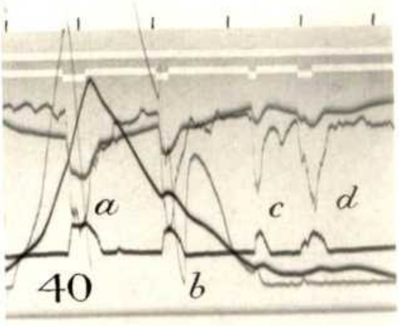
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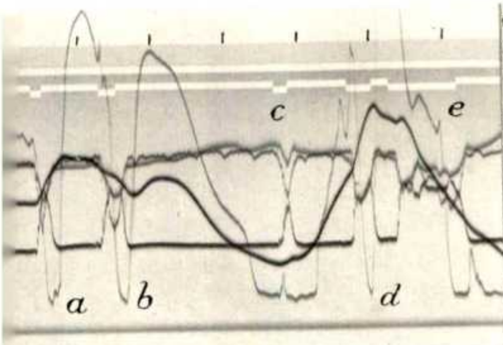

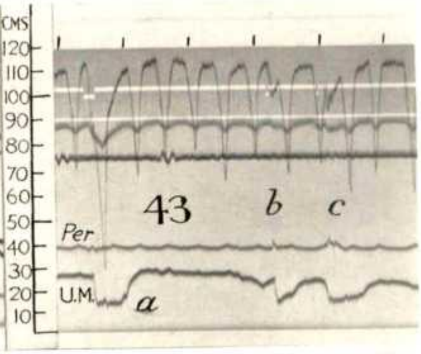
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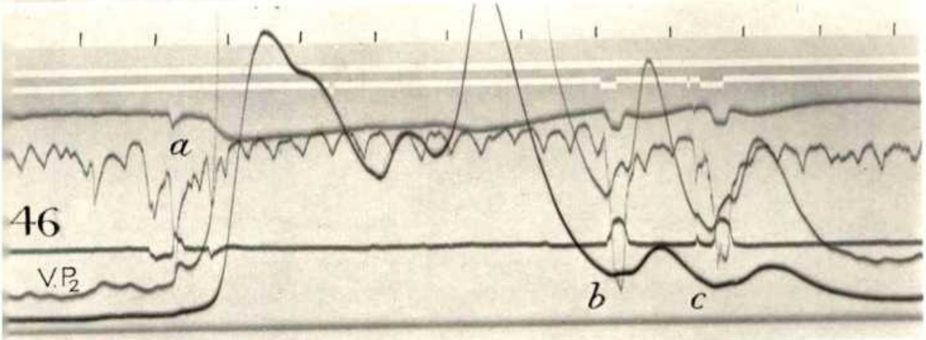
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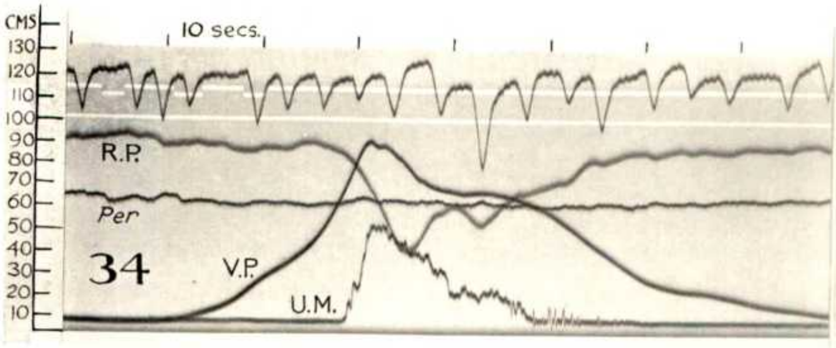

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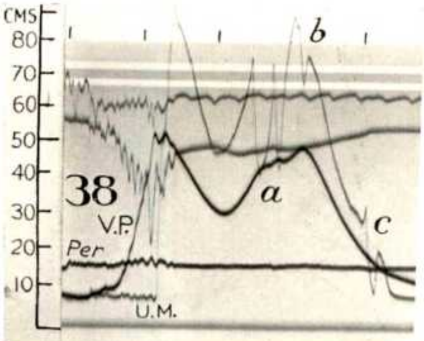

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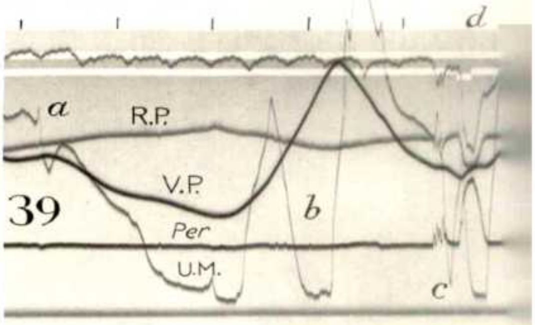

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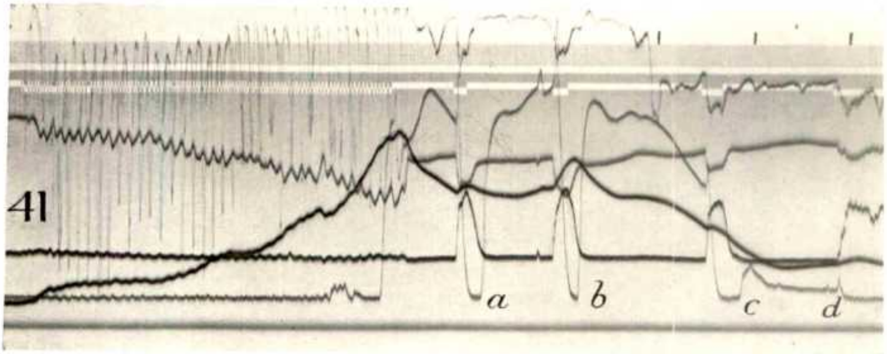

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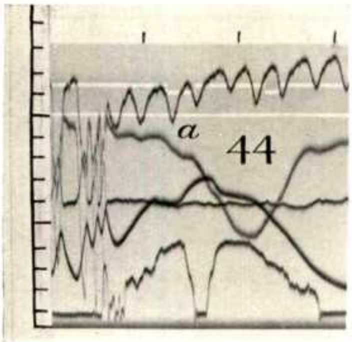

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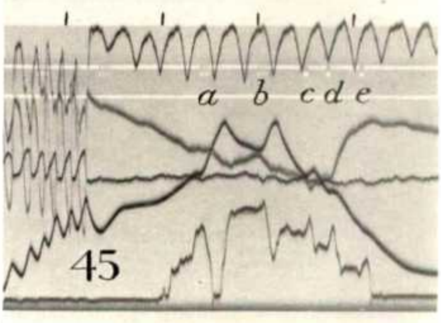

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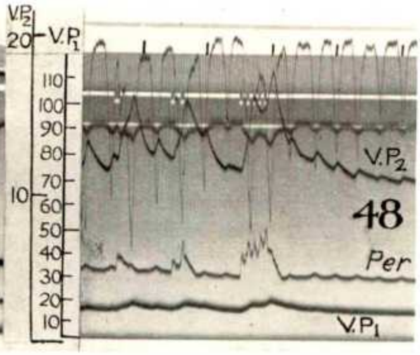

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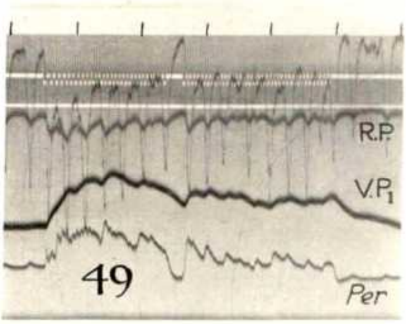

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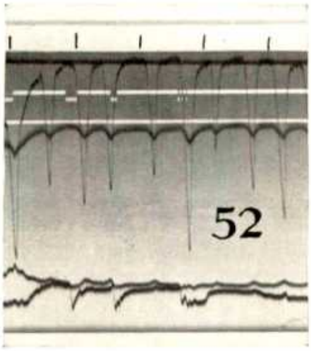

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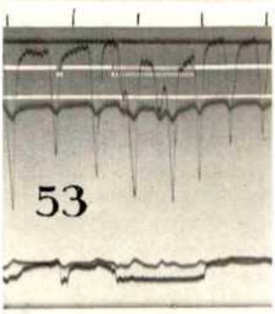

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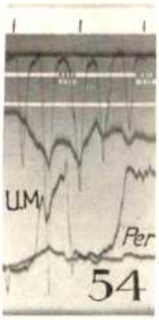

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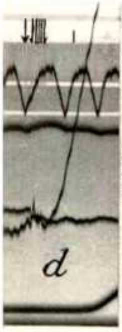

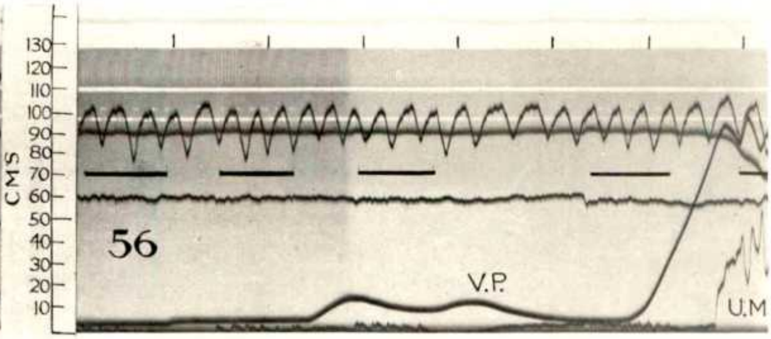

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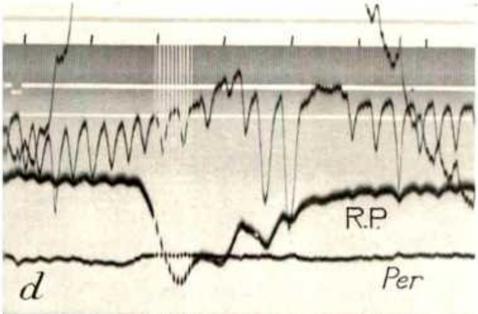

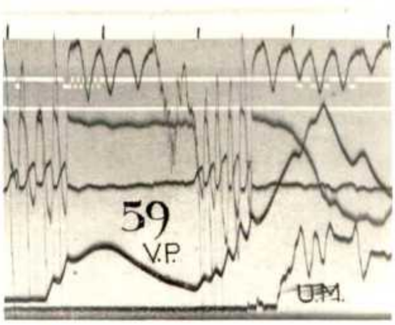

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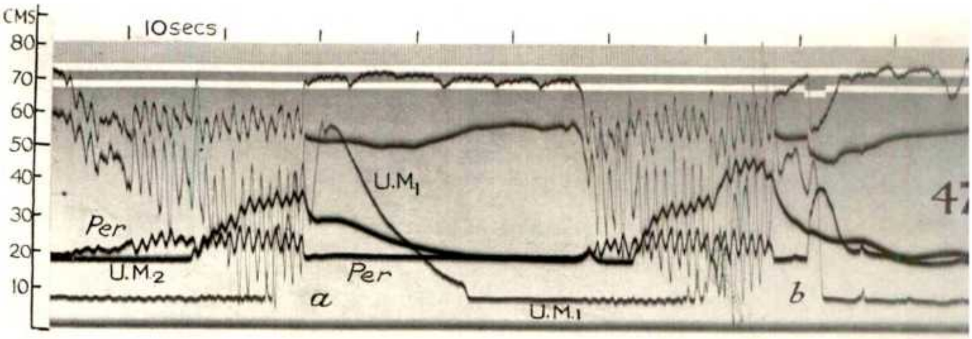

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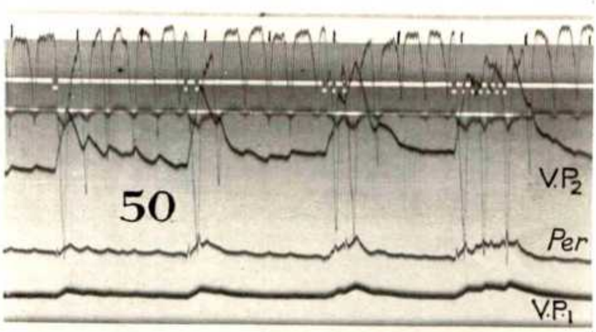

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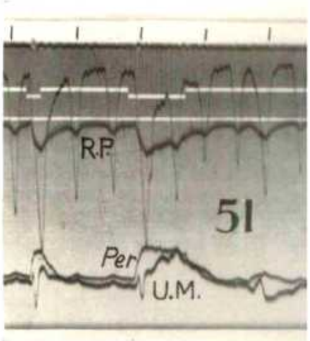

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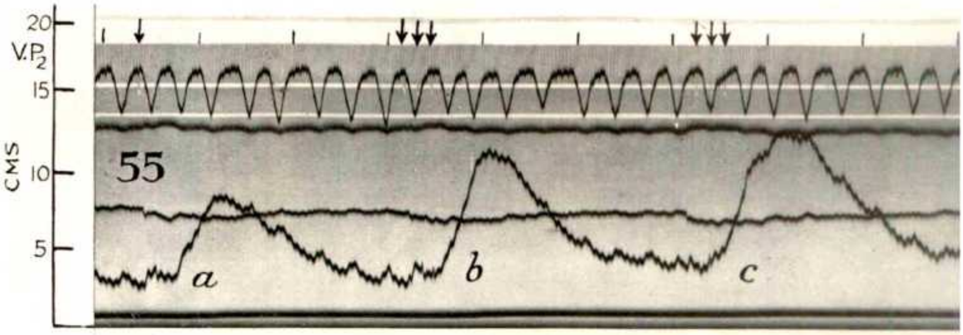

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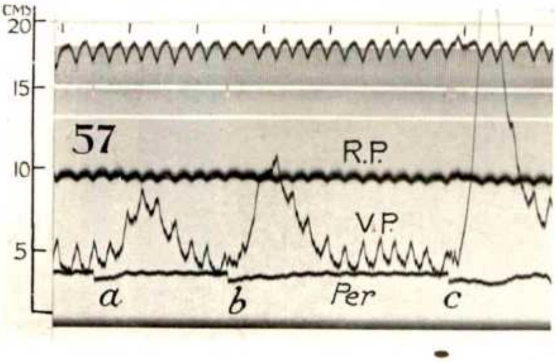

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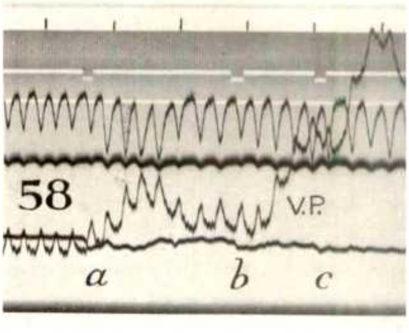

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## PLATE XVII.

FIG. 47. *Case* 4.—Both catheters withdrawn into urethra so that proximal heter, of which the manometer records by the thicker line $U.M._2$, lies with its orifice st outside the bladder while the outer catheter lies well beyond the region of the ternal sphincter and records by the thinner tracing $U.M._1$. Micturition is evoked by assage and at *a* is allowed to take its course. The second micturition at *b* is interpted by a scratch to the sole of the foot, of which the duration is shown by the break the white signal line. The orifices of the two catheters were separated by 6 cm. of ethra. Vesical pressure not recorded.

FIG. 48. *Case* 6.—Both catheters within the bladder. A single prick to right side glans penis at each downward movement of signal line. Constant volume 200 c.c. ension scale applies to figs. 49 and 50.

FIG. 49. *Case* 6.—Constant volume 350 c.c. A series of single pricks to sole of ght foot with lapse in middle of series.

FIG. 50. *Case* 6.—Single pricks to sole of the left foot. Direct continuation of . 48.

FIG. 51. *Case* 6.—Continuous dribbling discharge during filling, with urethral atheter withdrawn beyond region of external sphincter. Vesical pressure not shown. t the first fall of signal the sole of the right foot was pricked once, the second fall dicates the duration of a stroke along the outer border of the right foot. Resting vel of urethral manometer is shown in fig. 53.

FIG. 52. *Case* 6.—Continuous dribbling discharge during filling as in fig. 51, to now the effect of two separate single pricks to the left side of the glans penis conasted with that of three similar pricks in rapid succession.

FIG. 53. *Case* 6.—The effect of one prick to the left side of the glans penis ntrasted with a continuous series of such pricks, which caused complete cessation f discharge for fourteen seconds.

FIG. 54. *Case* 6.—As in fig. 53. Discharge increased by pressure on lower bdominal wall. A series of pricks to the right side of the glans provokes rapid and asting cessation of micturition.

FIG. 55. *Case* 5.—September 9, 1933. Constant volume 100 c c. Vesical ressure recorded through single large catheter. A single prick is applied to the base f the glans penis at each momentary displacement of the upper white signal line indicated by arrow). After the last series of pricks at *d* the vesical pressure rises apidly to a maximal vesical contraction and micturition occurred.

FIG. 56. *Case* 5.—September 10, 1933. Volume 100 c.c. The prepuce was noved rapidly over the glans penis several times in the duration of each horizontal lack line.

FIG. 57. *Case* 5.—September 2, 1933. Constant volume 100 c.c. A single prick o the glans penis is electrically recorded by each fall of the upper signal. At *a* and t *b* are recorded the effects of single pricks in rapid succession. Vesical pressure ecorded by single catheter.

FIG. 58. Case 5.—September 2, 1933. Volume 151 c.c. At *a* a prick was delivered to the outer border of the right foot. At *b* and at *c* a scratch to the heel of the right foot and at *d* a prick to the outer border of the right foot. In the subsequent maximal contraction 105 c.c. was discharged. Tension scale as in fig. 57.

FIG. 59. *Case* 5.—September 10, 1933. Volume 150 c.c. A prick to glans penis delivered with each fall of the upper signal.

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# PERCEPTION OF FLICKER IN LESIONS OF THE VISUAL PATHWAYS.

BY GILBERT PHILLIPS (UNIV. SYDNEY),

*Liston Wilson Fellow; Fellow of the Rockefeller Foundation.*

*(From the Neurosurgical Unit of the London Hospital)*

THE perception of flicker has received considerable attention in physiological laboratories, but hitherto has not been applied to the study of disease with the exception that Braunstein [1], in 1903, using an alternately black and white sectored disc, investigated flicker perception in cases of optic atrophy and optic neuritis (causes not stated), amblyopia, glaucoma, chorio-retinitis and hemeralopia. With central fixation he observed a decrease of flicker perception in many of these cases. The peripheral retina was not investigated, and localizing defects of flicker perception were not sought for. The present work is a preliminary study of the perception of flicker in cases of intracranial tumour.

The ability of patients to appreciate flicker has been estimated by the rate of light interruption at which a flickering light loses its flickering character and appears to the subject as a steady illumination. This rate of light interruption is critical and is known as the fusion frequency. It is profoundly influenced by the intensity of the light and the size of the area in which flicker appears [2]. It is also modified by the brightness of the background, by variation in the light or dark adaptation of the subject's eye, by the length of time the light is observed before a judgment is given as to whether it is flickering or not, and by the region of the retina on which the light is projected. It serves no useful purpose to the present problem to consider the quantitative aspects of these factors which influence the fusion frequency, since, with one exception, they have all been kept constant. The only variable has been the area of flicker. As this area increases the fusion frequency rises, the rise being greater, within limits, as the light is projected further into the retinal periphery.

It is now generally believed that this effect of increasing area is due to spatial summation in the retina [3]. Granit and Harper [4] have shown that central and peripheral retinal areas exhibit only quantitative differences in summative effects. They have pointed out that these differences are supported by histological evidence. Opportunity exists for summation in the human retina between bipolar, horizontal and amacrine cells, and the quantitative differences between central and peripheral summation are no doubt due to their mutual relations and to the convergence of receptors through them on to the final common pathways constituted by the axones of the retinal ganglion cells.

Fusion frequencies of flicker, both in large and small areas, at selected points in the four retinal quadrants, have been examined in this work.

## APPARATUS.

Determinations of fusion frequency have been carried out in a room from which it was possible to exclude all sources of light except that from two 60 watt lamps placed 3 ft. apart and at equal distances on either side of a point 4 feet perpendicularly above the subject's head. The background consisted of a piece of blackened linoleum, 10 ft. by 12 ft., set in a frame and attached to the wall behind the flicker apparatus. The flicker apparatus (fig. 1) comprised a small electric motor connected by a belt to a fan attached to one end of a shaft mounted on two ball bearings. The fan had two 90-degree opposed vanes to give equal phases of light and darkness. Attached to the other end of the

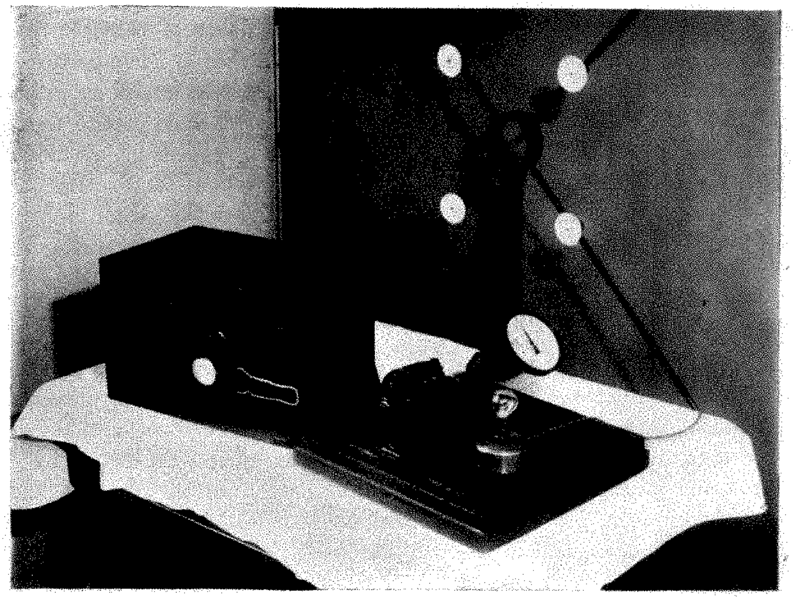


FIG. 1.—The apparatus used for determining fusion frequencies of flicker. The metal cover has been removed from the hardwood base to show the motor, the fan and the tachometer. In the background is the upright stand carrying four fixation discs.

shaft by a small spring coupling was an eddy current tachometer capable of recording on an illuminated dial the speed of the shaft from 5 to 30 revolutions per second. Immediately behind the fan was placed a 12-volt concentrated filament lamp mounted on a heavy lead base. This lamp was illuminated by a large capacity accumulator, the voltage from which was recorded by a Ferranti voltmeter and maintained constant by a small variable resistance. In front of the fan was mounted a Luc shutter to permit exposure of the light for any desired period. The whole apparatus was enclosed in a black-japanned metal cover. On the front of the cover and coinciding with the shutter aperture was an iris diaphragm and a milk glass screen. The diaphragm aperture could be varied to subtend visual angles of from one to four degrees at the subject's retina one metre away. The glass screen ensured by diffusion of light an equal light intensity over the whole area of the aperture.

Immediately in front of the diaphragm was a metal ring, 3½ in. in diameter, supported on a heavy stand resting on the floor. Through this ring the light beam passed to the subject's eye. Mounted on the ring at 90 degrees to each other and at 45 degrees to the horizontal were four rods carrying sliding pieces to which were attached white cardboard fixation discs. The sliding pieces could be moved along the rods to form angles of from 5 to 45 degrees with the light beam at the subject's eye.

The subject was seated at a table facing the apparatus, the chin resting on a metal support and the eyes one metre from the diaphragm aperture. With monocular fixation along the four rods the light beam could be projected to any desired point along the 45 degrees meridian of any of the four retinal quadrants. On a control table, out of the subject's field of vision, were centralized the light and power switches, the resistances for varying the motor speed, the shutter control and the voltmeters, and resistances for recording and controlling the background brightness and the intensity of the flicker beam.

## CONDITIONS OF EXPERIMENT.

*Selection of areas of light beam.*—If the observed area of the light beam is too large the fusion point becomes less critical. As the fusion point is approached, using apertures of 4 degrees or over, the central area of the light may fuse early while the periphery continues to exhibit flicker. This effect is more marked for peripheral than for central perception of the light, and owing to spatial summation in adjacent retinal neurones this circumferential flicker may even be seen to extend beyond the edges of the light aperture. It was desirable therefore to use a small aperture in order to make a critical judgment of the speed at which flicker disappears from the area as a whole. On the other hand sufficiently large visual angles were necessary to be seen by patients who had field defects for small test objects. With small areas too the rise in fusion frequency with increase in area becomes considerably less, and it is obviously an advantage in detecting any defect of retinal summation that this rise should be as great as possible.

It has been found that the optimum range to satisfy these conditions lies between 1·5 and 2·5 degrees of visual angle. 1·5 degrees is greater than the largest test object used on the campimeter in this Unit, namely 50/2000 or 1·43 degrees, and can be seen 30 or 40 degrees in the periphery by patients with marked defects in the visual field contours for 10/2000 or smaller test objects. With the 2·5 degree aperture inexperienced subjects have little difficulty in making a critical judgment of the fusion point even when the light is projected far into the periphery. In any one subject repeated estimations of fusion frequencies of constant apertures have not varied from the mean result by more than one light flash per second. Under the conditions described here an increase of aperture from 1·5 to 2·5 degrees has, in normal subjects, increased the fusion frequency from between 8 to 12 light flashes per second, depending mainly on the region of retina illuminated.

*Light adaptation.*—The absolute value of the fusion frequency for any light of constant area and intensity varies considerably with the condition of light or dark adaptation of the retina. With central fixation and a dark adapted retina the fusion frequency may be 8 flashes per second slower than with the retina adapted to the standard background brightness described above. With 30 degrees paracentral projection of the light this difference may be as great as 12 flashes per second. In this work, as a preliminary to making estimations of fusion frequencies, each subject has been permitted 5 minutes adaptation to background brightness. This time has been occupied in demonstrating coarse and fine flicker and fusion for both 1·5 and 2·5 degree apertures.

*Adaptation to flicker.*—The retina quickly adapts to flicker, the rate of adaptation being more rapid in the periphery. This quality necessitates equal time exposures of the flicker beam in estimating its fusion frequency. Constant time exposures avoid apparently lower readings in the periphery. For example, a light of 1·5 degree aperture exhibiting coarse flicker became fused after 3 seconds constant fixation at 30 degrees in the periphery. With 10-degree peripheral projection of the light, adaptation is slower (7 to 10 seconds), and the flicker appears finer and finer during this adaptation period. It finally disappears, but an accurate judgment of the point at which it does so is difficult. Comparable results, therefore, demand constant periods of light exposure of less than 2 seconds. During this exposure the rate of light interruption must also be constant. Short periods of light exposure are of advantage since absolutely steady fixation is only required for a correspondingly short time. If fixation is not steady a light which is just fused may exhibit flicker at its margin and thus produce an apparently higher fusion frequency.

It is important that the period of light exposure should not be shorter than one second. Granit and Hammond [5], working with 1 and 3-degree apertures and a central and peripheral fixation, found that the fusion frequency rose from the onset of exposure, at first rapidly and then more slowly, finally reaching a maximum in rather less than a second. In the work described here equal exposures of one second duration were used and the subject was required to judge whether flicker occurred at any period of the exposure.

A definite judgment was usually given as to the presence or absence of flicker on a single exposure, and it was only rarely when the light was being projected well out in the periphery that a second exposure was requested or an indecisive reply elicited.

*Fixation.*—Before beginning estimations the blind spots were mapped out in order to demonstrate steady fixation and guard against pseudofoveæ. No cases in which central vision was interfered with have been included.

## RESULTS.

*Normals.*—Creed and Ruch state in a recent article [6]: "From the somewhat confusing literature we are probably justified in concluding that flicker is more marked in the periphery than in the centre of the field of vision with moderate intensities of illumination and objects of moderate size, but that the contrary may often be found with small objects (subtending less than 1 degree or 2 degrees) and with intense stimuli." This statement shows the necessity for controls in the interpretation of results, and in obtaining controls the experimental conditions modifying flicker must be constant throughout. A sufficiently extensive survey of the normal retina should be made to include possible regional variations in flicker not only from centre to periphery, but from quadrant to quadrant. This has been done by examining in some detail the perception of flicker in three skilled observers and in the

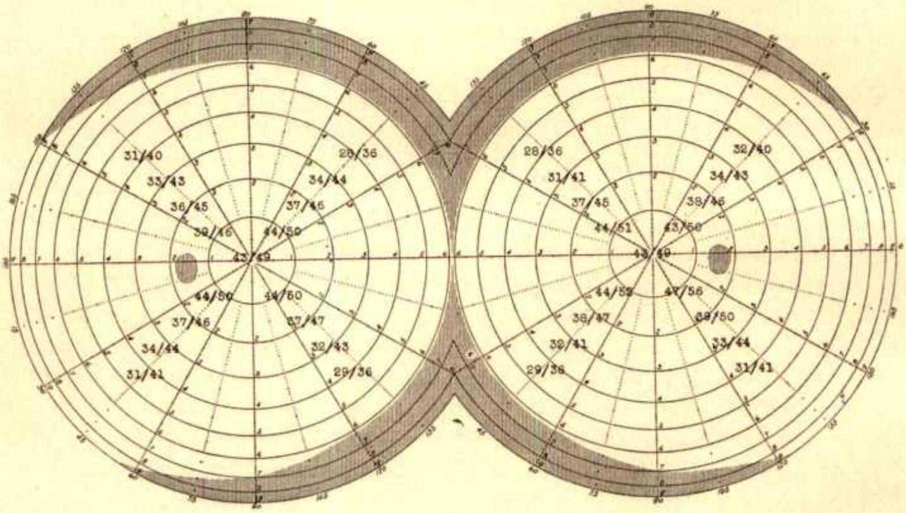


FIG. 2.—Fusion frequencies of flicker in a normal subject. Each pair of numbers represents the fusion frequencies of 1·5 and 2·5-degree light apertures respectively.

normal quadrants of patients with visual field defects. All factors modifying flicker were constant with the exception of the light aperture, which subtended an angle of either 1·5°, or 2·5° at the subject's retina. All four quadrants of each visual field were examined as far as 40° into the periphery. Seventeen points, 10° apart, were selected in the visual field of each eye, the fusion frequency for 1·5° and 2·5° apertures determined at each point and the results plotted on charts (fig. 2).

The results corresponded closely and confirmed several previous observations on flicker. There was always an increase in fusion frequency corresponding to an increase in area and this increase was, within limits, greater in the periphery. With the areas and light intensity used the fusion frequency for a constant aperture fell as the light was moved from 10° outward into the periphery, and also fell slightly as it was moved from 10° towards the fovea (fig. 3). This observation has been made under different conditions by Granit and Harper [4], Creed and Ruch [6], and Lythgoe and Tansley [7]. It is due most probably to antagonism between receptor sensitivity and spatial summation. Summation is at a minimum at the fovea and increases with increasing convergence in the periphery. Receptor sensitivity is at a maximum at the fovea and appears to diminish pro-

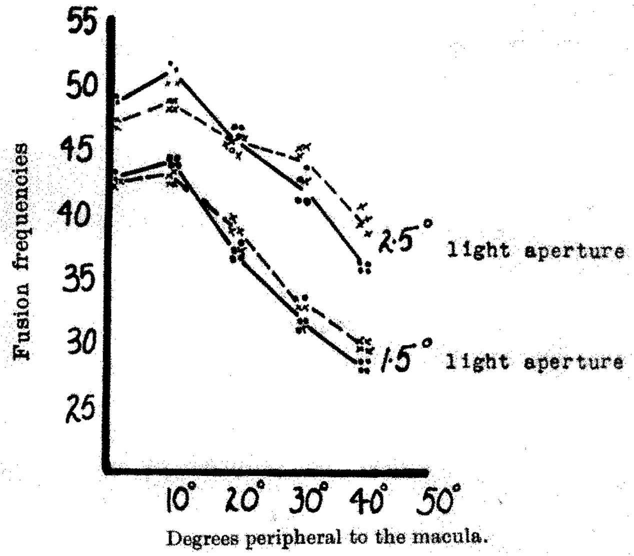


FIG. 3.—Fusion frequencies of flicker in the retinæ of two normal subjects.

Subject P.A.L. : +----+----+----+ Subject G.E.P. : ___·___·___·

gressively in the periphery. Summation increases the fusion frequency, while low sensitivity decreases it, and the point of minimum antagonism for a constant area and intensity appears to lie between the fovea and the 10° isopter. This point was not determined accurately since the points examined were 10° apart. It appears from fig. 3 that the highest absolute value of fusion frequency is at 10° from the fovea, but the value may rise higher somewhere between the fovea and 10° [7]. Between 10° and 30° spatial summation with increase in area becomes greater, or in other words the slope of the 1·5° aperture curve is steeper than that for 2·5°. With both apertures the fall in receptor sensitivity proceeds *pari passu*, while summation is facilitated by the larger area and thus the curves diverge. Beyond 30° the curves converge, probably due to the continued fall of receptor sensitivity after the maximum development of summation. In different individuals the absolute values of these curves may be slightly higher or lower but their mutual behaviour tends to be constant. The fall in the absolute value of fusion frequency beyond 30° was generally greater in the nasal fields (receptors innervated by the ipsilateral cortex) (fig. 2).

In the temporal fields there is a higher fusion frequency in the lower quadrants than in the upper. This observation is parallel with that made by Weymouth and others [8] who found that light perception was higher on the temporal and inferior meridians, and lower on the nasal and superior.

In determining the changes in flicker perception occurring in disease, the results shown in fig. 2 may be taken as a typical normal series. The maximum variation between any fusion frequency of this series and any other corresponding normal frequency determined under the same conditions is of the order of two or three light flashes per second. In disease the fusion frequency may be reduced by more than 50 per cent.

### Chiasmal Group.

*Case* 1. *Large intrasellar Rathke pouch cyst.*—Th. D., male, aged 39. There had been progressive failure of vision in the left eye for two years, but no subjective disturbance of vision in the right eye. At operation on July 21, 1932, the tumour was removed completely, a procedure made possible by section of the left optic nerve.

Before operation there was no perception of light in the left eye, while in the right eye the visual acuity was $\frac{6}{9}$. The field of the right eye before operation is shown in fig. 4 and displays a full field for the 1·73 degrees test object and a temporal defect, more marked in the upper quadrant, for the 8·6 minute test object. There was marked primary optic atrophy in the left eye with a deep cup and a well-defined lamina cribrosa. The right disc exhibited only very slight pallor.

On March 17, 1933, visual acuity was the same as before operation, but there had been a recovery of the contours of the field for the 8·6-minute test object (fig. 5). Except for a slight fall of visual acuity and a slight pallor of the disc this eye might be regarded as normal. Even with a 1·7-minute test

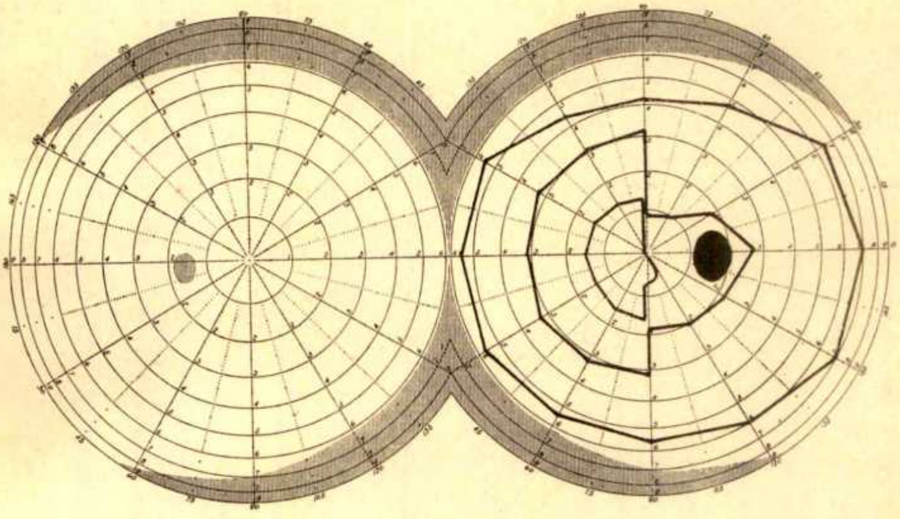


FIG. 4.—Visual fields of Case 1 one day before operation. Visual acuity of right eye $\frac{6}{9}$. Test objects: 1·73 degrees and 8·6 minutes, and 17·2 minutes (red).

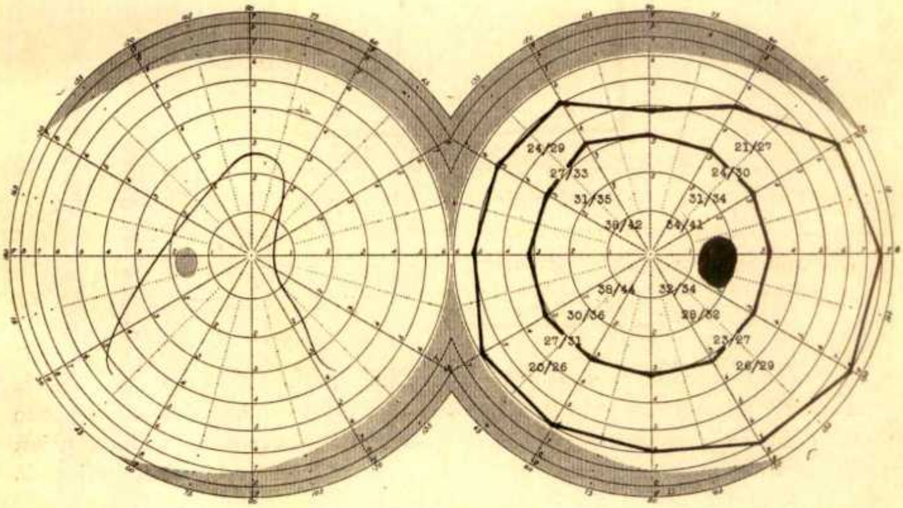
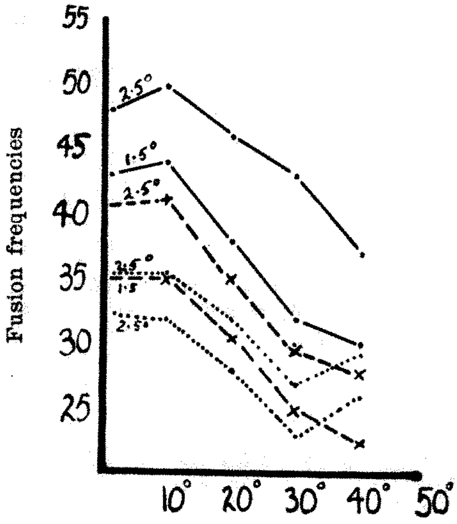


FIG. 5.—Visual fields and fusion frequencies of flicker in Case 1 eight months after operation. Central vision of right eye $\frac{6}{9}$. The fields are charted for 1·73 degrees and 8·6 minutes test objects.

object there was no field defect. In spite of this there was a fall in the fusion frequency of flicker in all four quadrants. Both 1·5-degree and 2·5-degree apertures were affected proportionally. As this benign lesion had been completely removed eight months previously the changes in flicker perception were evidently due to destruction of axones. This is in accord with the fact that, to judge from the endocrine disturbances, the lesion had been present for many years.

Another significant observation here and in other cases where there was chiasmal compression and evidence of optic atrophy was a local fall in fusion frequency between regions of higher frequency. In fig. 6 this local fall can be seen at 30 degrees in the lower temporal quadrant where the fusion frequencies are lower than at 20 degrees or 40 degrees. This local fall is prone to occur in the quadrant or quadrants in which the general fall of fusion frequency is most marked, and is no doubt due to local axone destruction at the point of maximal pressure by the tumour.



Degrees peripheral to the macula.

FIG. 6.—Fusion frequencies of flicker in the right eye of Case 1.
(Average curves of all four quadrants) : + - - - - + - - - - + - - - - +
(Right lower temporal quadrant only) : ..................................
Normal curves : ·______·______·______·

*Case 2. Intrasellar cystic chromophobe adenoma of the pituitary gland.*—C. A., female, aged 55. There had been a history of visual disturbance for twenty years. She had had to wear glasses and the left eye was said not to be as good as the right. For eighteen months she had had difficulty in reading. At operation on December 20, 1932, the cyst containing 4 c.c. of fluid and its capsule were completely removed.

Before operation the fields and acuity were as in fig. 7, and there were signs of primary optic atrophy of both discs more marked in the left. The left eye was not examined for flicker because of the involvement of macular vision. In the right eye before operation flicker could not be perceived in the upper temporal quandrant, while there was a marked fall of fusion frequency for both apertures in the lower temporal quadrant, accompanied by a slight fall in the nasal quadrants (fig. 7.).

A fortnight after operation there was a marked improvement in the acuity and field of the right eye and flicker perception, though grossly impaired, had returned in the upper temporal quadrant. There was in addition a slight rise in the fusion frequency of both apertures in the lower temporal quadrant (fig. 8) and in the nasal field.

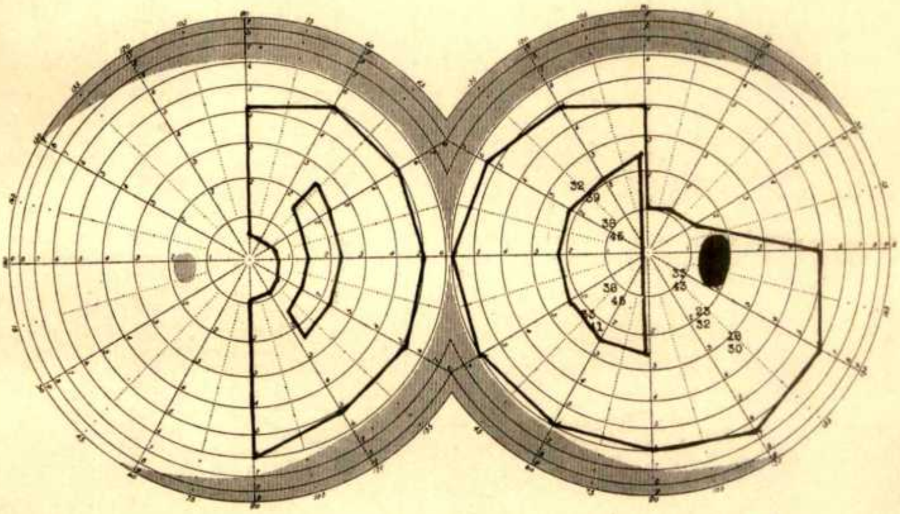


FIG. 7.—Visual fields of Case 2 one day before operation. Visual acuity of right eye $\frac{6}{36}$, of left eye $\frac{3}{60}$. Test objects: 1·73 degrees and 8·6 minutes.

The changes in fusion frequency observed in this case two weeks after operation are very closely allied to those observed in Case 1 eight months after operation, and in both cases, no doubt, there had been considerable axone destruction.

*Case* 3. *Chromophobe adenoma of the pituitary gland.*—P.M., male, aged 33. The tumour was removed subtotally on May 2, 1933. In this case there had been a complaint of failing vision in the left eye for twelve months. The patient had first noticed a "blankness" to the left of the left eye. He had had a "misty streak" in front of the right eye for four months before operation.

On examination there was severe primary optic atrophy on the left side with a well-defined lamina cribrosa. The right optic disc exhibited some pallor on the temporal side. The acuity was $\frac{6}{9}$ left and $\frac{6}{6}$ right, and the nature of the field defect four weeks before operation is seen in fig. 9. Fixation was unsteady in the left eye. At this time flicker fusion frequencies in the right eye were diminished in the four quadrants, slightly in the nasal but more definitely in the temporal field. Both apertures were equally affected. There was a

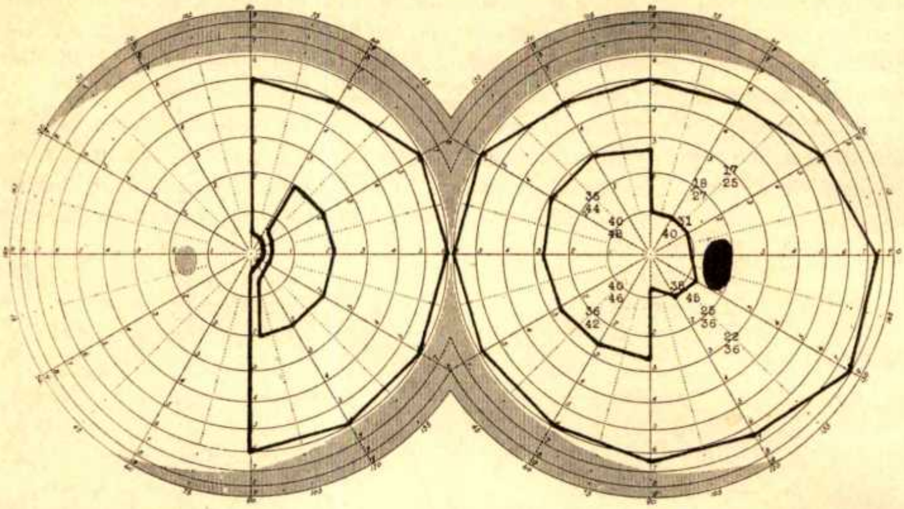


FIG. 8.—Visual fields and fusion frequencies of flicker of Case 2 fourteen days after operation. Visual acuity, right eye $\frac{6}{12}$, left eye $\frac{6}{60}$. Test objects: 1·73 degrees and 8·6 minutes.

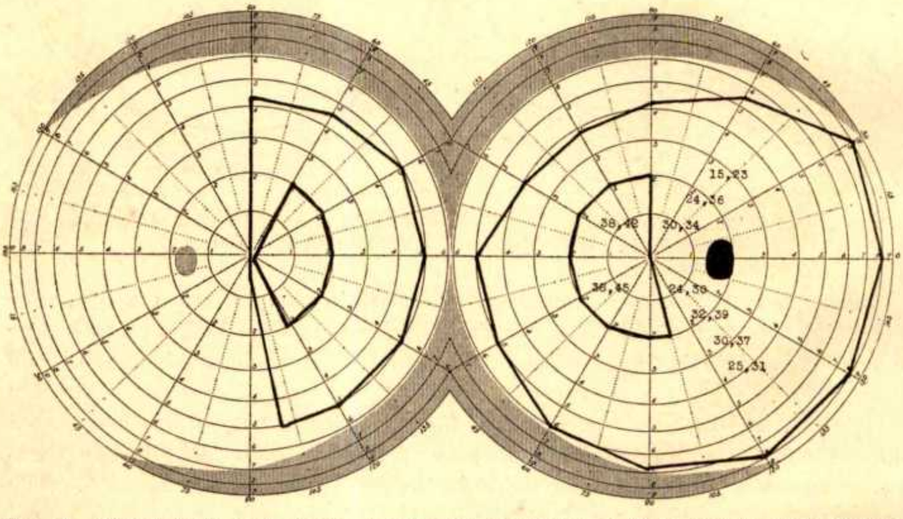


FIG. 9.—Visual fields and fusion frequencies of flicker in Case 3 four weeks before operation. Visual acuity of right eye $\frac{6}{6}$, of left $\frac{6}{9}$. Test objects: 1·73 degrees and 5·2 minutes.

marked local fall of fusion frequencies at 10 degrees in the lower temporal field. Two days before operation a central scotoma had developed in this area extending from the fixation point out to 10 degrees. Thirteen days after operation the visual acuity was $\frac{6}{6}$ in both eyes, and the visual fields had recovered considerably (fig. 10). Fixation was still unsteady in the left eye. In the right eye the fusion frequencies in the temporal field were much higher than before operation, and at 10 degrees in the lower temporal quadrant, where there had been the scotomatous defect suggesting a rapid advance in the lesion (9), the fusion frequencies were not very much below normal. This suggests that here the rapidly increasing pressure had impeded conduction without actually destroying the nerve-fibres. In the nasal field of the right eye there had not only been no improvement of flicker perception, but the fusion frequencies, especially for the larger aperture, had fallen slightly. The explanation here may have been that in some fibres which had been under pressure for a long time actual degeneration had finally taken place. Such degenerative changes would greatly diminish retinal summation, and thus the larger area would be more affected.

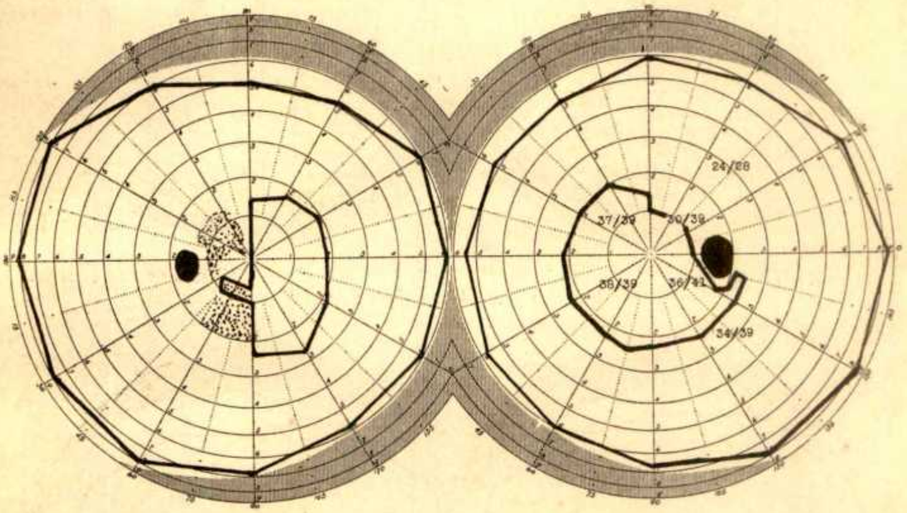


FIG. 10.—Visual fields and fusion frequencies of flicker in Case 3 thirteen days after operation. The fields are charted for 1·73 degrees and 5·2 minutes test objects. No trace of relative scotoma in right temporal field. Occasional scotoma in left temporal field near macula. Central vision $\frac{6}{6}$ in each eye.

*Case* 4. *Chromophil adenoma of the pituitary gland.*—J. O. H., male, aged 29. The tumour was subtotally removed on April 11, 1933. The history and acromegalic appearance of this patient indicated that the tumour had been present for some years. and at examination two years before operation a slight upper bitemporal defect of the small isopters was observed. Subjective visual failure, however, only appeared five months before operation. On examination there was slight temporal pallor of both discs, rather more marked on the left side. Visual acuity was reduced to $\frac{6}{9}$ in the right eye and $\frac{1}{18}$ in the left. There was a bitemporal defect, scotomatous in the left eye and peripheral and central in the right (fig. 11). The examination of flicker perception was precluded by the impairment of macular vision in both eyes.

Fourteen days after operation there was a considerable recovery of the visual fields, and the visual acuity was $\frac{6}{9}$ in each eye. The bitemporal defect could only be demonstrated by small test objects (fig. 12). Flicker perception was diminished in all four quadrants in both eyes. There were profound local

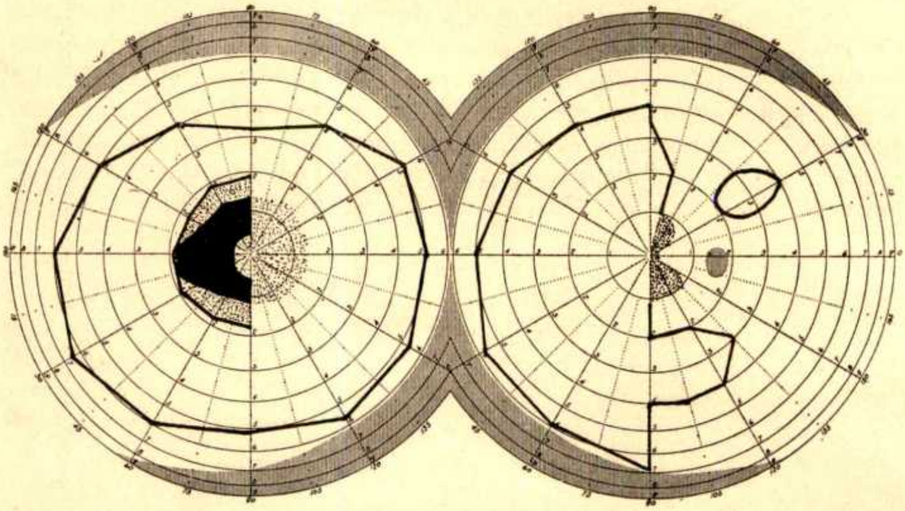


Fig. 11.—Visual fields of Case 4 immediately before operation. Visnal acuity of right eye $\frac{6}{9}$, of left eye $\frac{1}{18}$. Test object: 1·73 degrees.

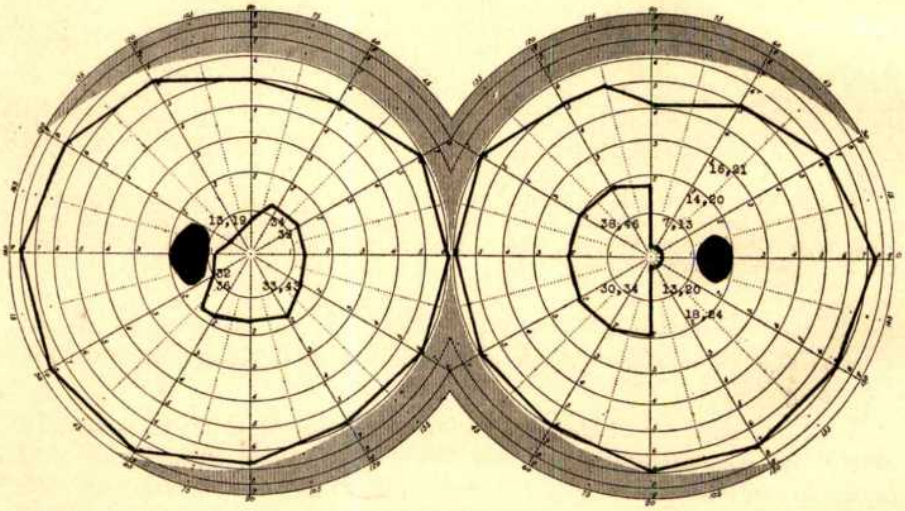


Fig. 12.—Visual fields of Case 4 showing fusion frequencies of flicker fourteen days after operation. Visual acuity of right eye $\frac{6}{9}$, of left eye $\frac{6}{9}$. Test objects: 1·73 degrees and 5·2 minutes.

falls in fusion frequency close to the temporal side of each macula, except at 10 degrees on the left lower temporal quadrant, and there was a rise toward the normal in the region of the temporal island in the right eye. Both apertures were affected equally. Here again the scotomatous nature of the visual defect suggested rapidly advancing axone compression, and after the relief of pressure the most marked flicker defects persisted where axone destruction had been greatest. When a tumour has only been partially removed (Cases 3 and 4) the remainder of the tumour is still able to produce some tension which may result in "decremental conduction."

Four other cases of chiasmal compression have been examined for flicker defects and they all confirm the results described in this section.

From these observations the following conclusions may be drawn about the effect of chiasmal compression on flicker perception. (1) Flicker perception is diminished; (2) this diminution may occur in the absence of any defect in the visual field (Case 1); (3) large and small areas are approximately equally affected; (4) the flicker defect generally appears to some degree in all quadrants of the visual field; (5) there are usually marked local falls of fusion frequency of flicker in the quadrant or half field most profoundly affected.

### SUPRACHIASMAL GROUP.

Flicker perception was examined after operation in four cases of parietal tumour in which the visual fields and acuity were normal. In two cases, both of them calcified gliomas, flicker perception was normal. In another, an extensive left fronto-parietal cystic tumour, flicker perception was impaired in the right homonymous fields, but was normal elsewhere. In the fourth case, after removal of a huge right parietal meningioma, flicker perception was impaired throughout the left temporal field only, the left nasal and the right half fields showing no abnormality.

These observations are obviously too few to justify any conclusions being drawn, but they indicate that flicker perception may be diminished in suprachiasmal lesions and that this defect may occur in one or both of the contralateral half fields in the absence of any defect for form. The degree of dissociation may be so great that a light and its circular form may be appreciated in the periphery without any appreciation of flicker even at very slow rates of light interruption. The few observations so far made indicate that in suprachiasmal lesions, in contradistinction to the chiasmal group, flicker in small areas is more affected than flicker in large areas.

These observations suggest that there is a dissociation between flicker perception and the form-movement perception of perimetry. No conclusions as to its cause are justified without further work.

These observations on flicker perception are preliminary to a more thorough investigation of the several problems which arise out of them. This field for research which has been revealed by the quantitative investigations of Ragnar Granit and his co-workers on flicker is extensive, and owing to the scarcity of suitable cases information that may prove valuable to the clinician can only follow an intensive survey of a larger series of cases. This introductory paper is submitted in the hope that such investigations will follow.

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# LEIODYSTONIA, AN ENDOCRINE-AUTONOMIC NEUROSIS OF THE TROPICS.

BY P. M. VAN WULFFTEN PALTHE,
*Professor at the Medical School, Batavia, Java (Dutch East Indies).*

LEIODYSTONIA is a malady which is characterized by a disturbance in the regulation of the vegetative functions, and especially by a lability in the tonus of the involuntary muscles. For clinical purposes the name leiodystonia[1] will serve as it summarizes the essential symptoms without prejudice to the still uncertain causes of the malady. French clinicians [1] have given the name " léiasthénie " to analogous conditions ; they have also spoken of "*asthénie des muscles lissés.*" As leiodystonia is not identical with the *léiasthénie* of the French the latter name cannot be employed.

Its chief characteristic is a variability of the tonus of the involuntary muscles. It is true that this lability of tonus generally occurs on a low hypotonic level, but other symptoms are due to a spastic dystonia. For the same reason it is less desirable—as I myself did in a previous article [2]—to name the malady after one of its symptoms. In leiodystonia the blood-pressure is nearly always low, but it may be sometimes high ; this is a feature of the disease.

Leiodystonia is not a continuous disease but rather a constitutional inferiority called into being, or at least accentuated, by a long residence of Europeans in low-lying tropical country. The symptoms appear and disappear according as unfavourable or favourable factors predominate. It has been possible to study it in a large number of patients during the last seven years.

## SYMPTOMATOLOGY.

A prominent symptom is the low blood-pressure; the systolic pressure fluctuates around the 100 mm., the diastolic around the 50 mm., not only in youthful persons but also in patients between 40 and 50 years of age. The action of the heart is tumultuous. Sometimes there is a slight enlargement towards the right and an accentuated second pulmonary sound. Vascular murmurs can be frequently heard over the larger arteries.

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[1] Leiomyodystonia would be more correct, but as by tonus, muscle tonus is generally understood, the omission of the adjunct "myo" is justified.

The patients have often a peculiar facial expression owing to their dilated pupils and the whiteness of their skin. The cutaneous blood-vessels are very sensitive to mechanical and emotional influences, and flushings and red patches come and go, more especially on the neck. Frequently there is slight œdema, not of the subcutaneous tissue but of the superficial layers of the skin over the tibiæ. Visceroptosis is common and the stomach is frequently filled with air owing to aerophagy. Attacks of profuse perspiration without cause, and of watery diarrhœa without pain, alarm the patient, and uncontrollable fits of sneezing may keep him awake all night. Epileptiform convulsions, sometimes followed by transient hemiplegia, are not rare. Finally, most patients become sexually impotent.

The chief subjective symptoms are headaches, lassitude, giddiness and insomnia, or, on the contrary, excessive drowsiness. Pains, especially in the chest and over the heart or between the shoulder-blades, and, in the case of women in the lower abdomen, an empty weak feeling in the stomach accompanied by palpitation of the heart, attacks of terror, with sensations of sinking away, of dying or of becoming insane, are very common. Singing in the ears and cloudiness of vision add to the patient's misery, and as a result he loses his self-control, becomes irritable and has sometimes uncontrollable fits of weeping.

The history of a typical patient may give a better picture of the disease than such a dry summary of subjective and objective symptoms.

A man, aged 46, came to the Dutch East Indies in his 30th year. In Holland his health was always excellent, but after some years in the tropics he began to feel less well. His own opinion was that he has become "nervous." This opinion he based on the fact that his symptoms were variable, for sometimes he felt well and fit for anything, but at other times he was perfectly miserable. He had then a sensation of being strangled and his heart beat violently, or rather his whole body palpitated, not only his heart. He became giddy, had a feeling as if he were sinking away, a feeling which terrified him, "I feel as if I were dying." This type of attack alternated with periods of extreme lassitude, and if he did not fight against it he could do literally nothing, even to lift his arm demanded too great an effort. If he struggled against it the attack of lassitude quickly passed off. When subject to these attacks he slept abnormally long and soundly, not only during the night but also by day. Every now and then he had attacks of profuse perspiration. Another troublesome symptom was that at the most inconvenient moments, and without any definite cause, his eyes filled with tears and he had uncontrollable fits of weeping. As he had also pains all over his body and especially a violent pressure in his head, it is not surprising that this man, who had hitherto always done his work well although he had lately had some difficulty in concentrating his thoughts, should finally become desperate and call in medical help. It was, however, his wife who insisted upon it, as the patient thought it unworthy of a man to go to a doctor with such vague nervous complaints.

On examination there was no evidence of serious organic disease. The patient was a well-built man; his heart, lungs and kidneys were normal. The tendon reflexes were brisk. The pupils, which were remarkably wide, reacted promptly but insufficiently to light or on convergence, and quickly dilated again though the stimulus persisted. The retinal arteries were dilated almost as wide as the veins, and the discs were somewhat rose-coloured. No other changes were visible in the fundi. The most pronounced changes were found in the peripheral circulation; red spots and flushes were everywhere visible, more especially where his clothes had pressed. If a hand was laid for a single moment on his back a clearly visible impression of it in white was seen. A light touch was sufficient to cause a contraction of the cutaneous capillaries, a contraction which quickly passed into relaxation, for after a few seconds the mark became red. This peculiar dermography was still more striking when the skin was stroked with the handle of the percussion-hammer: first a white line appeared which immediately became bright red and was bordered by white rims, each about twice as broad as the central red line. Irritation of the skin anywhere was followed by alternate cramp and paralysis of the cutaneous blood-vessels. Red spots also appeared spontaneously.

The blood-pressure of this patient, whose heart was perfectly normal, was remarkably low for a man of his age. When we first took it after having adjusted and increased quickly the pressure in the armlet, thus exercising a strong stimulus on the arterial wall, the maximal pressure was 115 mm. Hg, but later, by avoiding as much as possible stimulation of the arterial walls, the systolic pressure fluctuated between 95 and 105, and the diastolic between 55 and 60.

From this description it is obvious that each of the various complaints and objective symptoms had in itself little that was characteristic; looking at them separately one might conclude, and it has been done too frequently, that the patient was an ordinary neurasthenic. But this man did not show the usual neurasthenic attributes; he regarded his complaints calmly and objectively, they were not an integral part of his personality nor bound up with it, and they exercised no continuous influence on his thoughts and actions, in short, there was no neurasthenic "character." It was necessary to compel him to go to the doctor, and he came accompanied by his wife, who had to urge him to say what he felt, because he was really ashamed of his symptoms, which he regarded as nervous. In short, he was the antithesis of the "man with the notebook" in which all complaints are precisely described in case the patient should happen to forget a single one. He did not pity himself, he felt it annoying to be ill, he accused neither persons nor circumstances, and did not ascribe his illness to "overwork." In short, he regarded his illness as something essentially strange, a temporary disorganization which he thought would disappear when he was in other circumstances. Something quite different, therefore, from the chronic neurasthenic, the "homme à petits papiers" who runs from one doctor to the other and cherishes his symptoms as valuable weapons in the struggle of existence; the terror of all neurologists even in the tropics.

Too much emphasis cannot be laid on the fact that one should never diagnose leiodystonia from any of the separate symptoms described above; not one of them, not even the low blood-pressure, is pathognomonic. It is true that the blood-pressure is always low, or it might be better to say that it fluctuates at a low level, but we must not see in every low blood-pressure a leiodystonic disturbance. In perfectly healthy persons a low blood-pressure may be sufficient for the circulatory requirements. In genuine leiodystonia, under favourable circumstances (for example, a sojourn in the mountains) all the symptoms may disappear, but the blood-pressure does not change.

It is not necessary in order to diagnose leiodystonia that all these complaints and symptoms should be present simultaneously and in equal intensity. This is rare, for generally one group of symptoms predominates and the others become apparent only after long observation and patient inquiring. These symptom-complexes, which are sometimes so dominant that they are described as special diseases, must now be dealt with in greater detail.

*The feelings of terror.*—This is described by the patient as a sensation of sinking away, of dying, as if life were flowing away; sometimes also as if his mind were going and he was becoming mad. There is a real terror of death and is felt as such by the patient. It occurs particularly when the patient is at rest, and not under the influence of psychic and physical stimuli. The attacks are preceded by a sensation of giddiness and of palpitation throughout the body. In this state the blood-pressure is extremely low and vascular murmurs are audible everywhere. Everything indicates that the circulation is insufficient owing to a leak in the peripheral arterial system and congestion of the veins. There may be real danger to life. Then comes the feeling of terror, which may perhaps be regarded as a useful biological reaction, for as a result of it substances are secreted into the blood which increase the tonus of the vascular walls and thus raise the circulation to its old level. One thing is certain, that the feeling of terror arises when it is necessary and disappears when the danger is over. It lasts only a short time and afterwards the patient feels better than he did before. The circulation also improves. Between the attacks the patient has no fears; he suffers as little from an anxiety neurosis as he does from neurasthenia.

*The ocular symptoms.*—The widely dilated pupils give the patient a peculiar appearance. To a strong light and on convergence they contract quickly but only in a slight degree, and even if the stimulus is continued they dilate again immediately. Loeper and Bauman [1] regard this as a constant sign in their "leiasthénie." In my cases it was seldom absent.

Symptoms of asthenopia are common and the patients complain of the disagreeable effect of bright daylight. In a few cases the optic discs were pinkish and the arteries in them were dilated, but never to such a degree as to suggest a choked disc such as Flandin and Gallois [3] have described.

*Gastro-intestinal symptoms.*—The gastro-intestinal symptoms commonly associated with leiodystonia often have an organic character, and consequently the patients usually call in a general practitioner or visit an internist. It is certain, however, that in the early stages at least there is no organic lesion. No matter how closely the symptoms may resemble those of gastric or duodenal ulcer, colitis or sprue, closer inquiry shows that the special features of these diseases are absent. No trace of inflammation or other changes, as atrophy of the mucous membranes, can be found. The changeable nature of the symptoms and the sudden cure which frequently follows a change of climate, also indicate the functional character of these symptoms.

These symptoms can be attributed to a hypersensibility of the autonomous reflex system of the intestinal tract. Some have a spastic character suggesting colitis spastica, and others are due to lack of tone, as the enlarged dropped stomach. There are also anomalies in the movements and the secretions of the intestines; obstinate constipation alternates with watery diarrhœa, without tenesmus and without mucus or blood. This hyperexcitability is clearly demonstrated by the reactions of the patients to slight and harmless stimuli; the first whiff at a cigar makes him giddy and induces an inclination to vomit, and a mouthful of coffee makes him hasten to the water-closet.

The patients have a number of other complaints of a more subjective nature. A disagreeable feeling of looseness, emptiness and heaviness in the stomach torments him at the most inconvenient moments, a feeling as if he were hollow and hungry frequently follows a meal which he has thoroughly enjoyed. In such a condition the stomach is filled with air and there is a moderate meteorism. If they are observed unawares it may be seen that these patients frequently swallow air, an action of which they are not conscious and consequently deny. It seems that the stomach distended with air is more comfortable than the feeling of loose emptiness, although it produces all kinds of discomfort later on.

This intestinal syndrome is often associated with cardiac and vascular symptoms, which is by no means surprising in view of their common origin. Organic affections of the intestinal tract, as colitis or chronic appendicitis, may determine the appearance of leiodystonic symptoms in other systems.

*Cardiac and vascular symptoms.*—The vascular syndrome is the most characteristic feature of leiodystonia. The low level and the variability of the blood-pressure is the symptom which attracts most attention, as it is the one which can be determined most clearly and objectively. This low, fluctuating blood-pressure is never absent, but one must not be satisfied with taking the blood-pressure once, and no conclusion should be drawn from the first visit to the doctor, when the pressure readings are often 10 to 20 mm. above their real level.

The vascular syndrome in leiodystonia, however, does not consist in a low blood-pressure only. The heart beats tumultuously, as in beri-beri, although the impulse is diffuse. In a few cases there is a slight enlargement to the right and an accentuated second pulmonary sound. The pulse is generally rapid and forcible. Murmurs can be heard over the larger arteries, as the femoral. Complaints of palpitation, inability to breathe deeply, pains in the chest and in the region of the heart, are common. All these symptoms resemble the circulatory disturbances in beri-beri, as described by Wenckebach and Aalsmeer [4]. The resemblance becomes still more striking as in leiodystonia too the circulation is paradoxically influenced by adrenalin. After an injection of 1 or ½ c.c. of a 1 : 1000 adrenalin solution, the heart begins to beat more tumultuously; the systolic blood-pressure remains the same or diminishes a little, but the diastolic falls until it can no longer be measured. The pulse is rapid and firm. Murmurs can be frequently heard over the smaller arteries, as the radial and dorsalis pedis, and over the larger arteries, as the femoral, they become very loud and acquire the sharp character of a pistol-shot.

A European, aged 26, who had already been five years in the tropics, during the last year began to be troubled with giddiness and attacks of faintness. He also complained of singing in his ears and at times of dimness of vision. A sensation of sinking away preceded short periods of absolute unconsciousness. Extreme lassitude, unnatural drowsiness, vague pains in his head and occasional palpitations completed the picture. All these symptoms became much worse when he took no exercise.

The objective symptoms were dilated pupils, white-rimmed red dermography, rapid pulse, brisk reflexes and slight pretibial œdema. The heart was not enlarged and its sounds were normal. The systolic blood-pressure varied between 150 and 130; the diastolic remained at 75. Directly after an injection of ½ c.c. of a 1 : 1,000 solution of adrenalin the blood-pressure was 145/90, after five minutes it was 145/75, after ten minutes 140/30, and after fifteen minutes systolic was 140, and diastolic could not be measured. Loud murmurs of pistol-shot character were audible over the brachial and crural arteries. The action of the heart was agitated, there were generalized palpitations and the visible veins were congested.

Latent leiodystonic disturbances may be revealed by enfeebling illnesses or intoxications. One cigar, even the first pull at a cigar, may produce giddiness and an inclination to vomit, cloud the consciousness and induce palpitations.

The question arises whether the similarity between the functional circulatory disturbances in leiodystonia and in beri-beri has a deeper significance; in other words whether they are both—though perhaps in a different degree — due to one and the same mechanism. Wenckebach [5] has suggested that the circulatory disturbances in beri-beri are due to two factors, viz., a dilatation of the smallest ramifications of the arterial system and consequently a flooding under high pressure of the veins and the right heart, and secondly a degeneration of the heart muscle.

Degeneration of the cardiac muscle does not occur in leiodystonia and therefore the circulatory disturbances associated with it have never serious consequences. The former factor, however, by which the scuppers of the arterial periphery are opened, is present in the case of leiodystonia; in this respect the circulatory disturbances in leiodystonia are identical with those of beri-beri.

*The cerebral symptoms.*—Cerebral symptoms appear in three forms: (1) As migraine; (2) as short periods of unconsciousness with or without convulsions; and (3) as loss of consciousness followed by a transient hemiplegia. In earlier articles [6] I have shown that such an attack of hemiplegia in a young person, without organic disease of the heart, vessels or kidneys, with a low blood-pressure, in the absence of syphilis and with nothing to suggest a tumour, multiple sclerosis or encephalitis, must be due to functional circulatory disturbances in the brain. This temporary disturbance is due to the association of cerebral vascular spasm with a low blood-pressure. Descriptions of a few cases may make this clearer.

The first patient was a young man, aged 24, who came to the Dutch East Indies for the first time two years ago. According to information supplied by those who knew him, he had already had several fits of "unconsciousness" which lasted from one and a half to two hours, and which were not accompanied by convulsions or spasms. He could say little more about these attacks than that they began with a sensation of cold and giddiness. A doctor who was called in when he was seized with the last attack had him removed to the hospital.

On examination, he had a left-sided hemiparesis, including the lower muscles of the face. With his left arm he could perform a few awkward movements only. Deep sensibility and stereognosis were disturbed in the left hand, in which there were also violent spontaneous pains. The abdominal reflexes could not be elicited on the left side. The left leg was also paretic and its tendon reflexes were exaggerated with ankle clonus; the reflexes of Babinski and Rossolimo were positive. The patient was dysarthric and stuporose, and complained of headache.

This was a classical example of a hemiparesis, the result of a lesion in the region of the right internal capsule extending into the thalamus. Further examination revealed no organic disease; his heart and blood-vessels were normal, his blood-pressure was low and the functions of the kidneys were unaffected. There were no signs of increased intracranial pressure. His temperature was normal. The patient denied venereal infection, and the Wassermann reaction in the blood and in the cerebrospinal fluid was negative, as was also Nonne's reaction. There was no pleiocytosis.

Formerly he had never been really ill. He did not drink, but smoked excessively. His occupation necessitated a busy, hustling existence. The heat where he worked in Priok Harbour (Java) is unbearable, and he ascribed his attack to it. Within twenty-four hours all his symptoms had disappeared, and he had become quite clear mentally. The following day he was up and about, but was still ataxic in his left arm and complained of spontaneous pain in it. The pathological reflexes in the left leg had disappeared but his face was still asymmetrical.

Two months later, after working for a long time in the heat, he was proceeding homewards on his motor-bicycle when his right side became paralysed and he fell. This hemiparesis lasted about an hour and had disappeared when we saw him. He was still a little drowsy and spoke with difficulty, but what immediately attracted attention was symmetrical snow-white discolouration of his legs to the middle of the calves. His feet and the lower part of his legs were cold and he complained of violent pain in them.

There was obviously a disturbance of circulation in the brain combined with vascular cramp in the legs. This vascular cramp recurred in the course of the following months when the patient was on his way to Holland and caused, when he was on board ship, gangrene of one of the toes. In Holland he gradually improved (according to the patient, this was due to his having stopped smoking) and he returned to the Dutch East Indies apparently cured. He lived now very quietly, had easier work, neither smoked nor drank, and everything went all right until he participated in a rather "wild" night. Emerging from a night club he collapsed, vomited and was unconscious for half an hour. When he recovered consciousness his right side was again paralysed and he was unable to speak. On this occasion also the hemiplegia disappeared in about twenty-four hours.

Another patient was a man, aged 38, who has been ten years in the tropics. He came under observation in 1927 owing to complaints of lassitude and impotency. There was no organic disease, but his blood-pressure was very low (about 100 mm. systolic). The vasomotor system was very labile: he complained of dead fingers when swimming, attacks of profuse perspiration and watery diarrhœa. In the beginning of 1932 he had his first stroke, which began with headache, giddiness, vomiting, walking like a drunken man and repeated attacks of unconsciousness which he spoke of as "falling asleep." The doctor then consulted found facial paralysis on the left side, dysarthria, increased reflexes and a hard pulse. As he did not know the previous history of the case and the blood-pressure was 200/140, he diagnosed an angiospastic lesion as a result of essential hypertension. Within a few days all the symptoms vanished and the blood-pressure was 100/30. Fourteen days after this attack I was able to examine the patient and found typical leiodystonic symptoms. The systolic blood-pressure was 96 and the diastolic 56. The reaction to adrenalin was slightly but unmistakably paradoxical.

This attack was followed four months later by a second, much slighter and of shorter duration.

This patient is interesting for two reasons; in the first place because he is a very moderate smoker, and secondly, because immediately after the first stroke his blood-pressure was for a short period greatly increased as compared to its usual low level. I believe that heavy smoking combined with a general lability of the autonomic nervous system is one of the factors that can bring about these transient attacks of hemiplegia, but Külbs [7] certainly goes too far when he sees in the abuse of nicotine the only cause.

A raised blood-pressure during and immediately after a stroke is common in "ordinary" apoplexy and indicates the extraordinary reflex sensitiveness of the vascular walls. It has been suggested [8] that this is a reaction on the part of the body to maintain, by means of the increased pressure, the circulation through the contracted cerebral arteries.

I have seen at least ten leiodystonic patients with cerebral symptoms such as are described above. In some of these angiospastic conditions in certain parts of the body, as white discolouration of the legs and dead cold fingers, alternated with general vascular atony. The combination of the two factors—spasm of the cerebral arteries and low blood-pressure—must be held responsible for the cerebral lesions.

All the symptoms which have been described separately in the ocular, the intestinal, the circulatory and the cerebral syndromes, together with the mental and physical abnormalities revealed by examination, should be regarded as a whole; they characterize one disease, leiodystonia, which in intensity and frequency reaches its height in the tropics. No one group of symptoms can be regarded as distinct or described as a special disease, however strange it may seem to place diarrhœa and hemiplegia, wide pupils and headache, in the same pathological unit.

As already said, leiodystonia is a latent constitutional inferiority which becomes manifest under certain unfavourable circumstances, and which disappears totally or partly when the factors which determined its manifestations have ceased to exist. Many arguments might be advanced to show that long residence in a tropical lowland may cause certain changes in the vegetative functions, and in particular in those predisposed to the malady called leiodystonia. This predisposition may exist in Europe as anomalies of the vegetative system, and in the tropics persons so affected may quickly show signs of leiodystonia. Vulnerability to tropical influences may also be acquired, and may be caused not only by the heat but also by an unhygienic manner of living (little sleep, excess in alcohol and tobacco, and little physical exercise), or by exhausting illnesses.

Various investigations have been made in the disturbances of the vegetative functions of Europeans living in the tropics; Radsma [9] found that the daily fluctuations in the carbonic acid content of the alveolar air was much greater than in temperate zones. In the afternoon there is an increase between 4 and 5 o'clock, and in the morning generally a diminution. Also the range over which the $CO_2$ tension varies in each individual is also greater than in Europe.

Radsma [9] also found that the reaction of the morning urine, in the case of Europeans in the tropics, is much more alkaline than in Europe. This shifting reaction is totally absent with the native population.

Neuhausz in 1893 showed that the average body temperature in the tropics is higher than in temperate zones. Radsma, who examined the daily temperatures of seventeen young Europeans, was able to confirm this. He found that smoking a single cigar increased his own temperature a few tenths of a degree.

The basal metabolic rate in Europeans in the tropics is also lower than in temperate climates. Knipping [13] found an average of −6·5 per cent., Teding van Berkhout [12] of −5·4 per cent. Benedict and Williams of −3 per cent., as compared with the standard figures of Harris and Benedict. Radsma also found the rate on the average 6 per cent. lower. This lowering of the basal metabolism cannot be ascribed to reduced albuminous nutriment. All indications go to show that it is brought about, directly or indirectly, by climatic factors.

Very little is known of the influence of the tropics on the blood-pressure of Europeans. Kiewiet de Jonge [10] found it was lower on the whole, but he was careful in coming to conclusions. Radsma, who measured the blood-pressure in forty persons between 20 and 30 years of age, obtained an average value of 110 mm. mercury for the systolic pressure. The American statistics give the average normal of 124 mm. for this age, and according to Halls Dally [11] the average level in England for persons between 20 and 30 years is 125 mm. Radsma recorded the blood-pressures of 12 persons within three months of their arrival in the tropics and again after two years. On an average the pressures under similar conditions had fallen 6 mm.; in two the pressures had remained the same, in all the other cases a fall had occurred. Radsma believes, however, that the number of persons examined was too small to justify the conclusion that in Europeans the blood-pressure is lower in the tropics than in temperate zones. Investigations by Knipping [13], and by Roddin and Cooper, also show that blood-pressures of Europeans fall when they are transferred to tropical climates.

I am personally convinced that in persons of all ages the blood-pressure is lower in the tropics than in Europe. This is especially so in persons with essential hypertension, in many of whom the pressure becomes normal after a residence in the tropics.

These physiological investigations have definitely shown that there is a greater lability of the vegetative functions in tropical climates. In persons predisposed to this lability, or under the influence of detrimental factors (diseases, intoxications), tropical influences can lead to the appearance of symptoms to which the name of leiodystonia has been given. There is much to support the view that the point of attack of this tropical influence must be sought in the endocrine-autonomic apparatus. The human powers of adaptation, however, are very great. Thousands of white people can live healthily in a tropical climate, and many when they first develop symptoms of disease may recover their health even if it is somewhat labile. Only very few require a speedy return to a temperate climate to regain their health.

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## NOTICES OF RECENT PUBLICATIONS.

*A Textbook of Neuropathology.* By ARTHUR WEIL. London: Henry Kimpton. 1934. Pp. 335. Price 25s.

This book is a concise and clear exposition of the essentials of neuropathology. It pays special attention to what might be called the general pathology of the nervous system, and gives fuller accounts of the chemical composition of nervous tissue and the processes of myelin disintegration than any other book of this kind. The sections dealing with post-mortem changes and the results of fixation are of special value. The chief pathological changes in ganglion cells and the reactions of different lipoids are set out in tables, greatly to the student's convenience. There are also useful diagrams of the distribution of the cerebral arteries. Elsewhere the book follows more conventional lines. The descriptions of the different forms of cerebral and spinal disease may err on the side of brevity, but we have few other faults to find with them. The introductory remarks to several of the chapters, such as those on inflammation and intoxication, are so apposite that we regret that more has not been said on the broader pathological aspects of cerebral vascular disease and cerebral tumours.

An appendix gives useful hints on post-mortem technique and staining methods, as well as tables of brain weights in relation to age and size of head which are useful in assessing normality.

The book is illustrated with over two hundred photomicrographs, most of which are excellent.

Altogether it is a valuable little book of which the only criticism we would make is that undue stress is laid on paralysis of the vascular nerves as a possible cause of lesions of the nervous parenchyma in such different conditions as carbon monoxide poisoning and concussion of the spinal cord. The results of total ablation of the vascular efferent nerves in animals seem to be wholly against such a theory.

*Neuropathology.* By WALTER FREEMAN. Philadelphia and London: W. B. Saunders Company. 1933. Pp. 349. Price 25s.

In this volume the author deals with the subject of neuropathology chiefly from the histological standpoint, and within this field he has given us a well-informed and reasonably full account of the subject. But the neglect of more theoretical sides of the subject, such as the pathogenesis of disease and the causation of symptoms, robs the book of much of the interest which the subject should have for neurologists. Only about 20 pages are devoted to diseases of the spinal cord. No doubt its simpler structure makes long descriptions unnecessary, but this does not wholly explain the very small space devoted to it. Thus vascular diseases and tumours of the spinal cord are scarcely mentioned, and the spinal lesions of acute disseminated encephalomyelitis and rabies are completely omitted from the survey of these diseases. More attention might also have been devoted to the naked-eye appearances of tumours of the brain and to the mechanism of intracranial pressure.

In several of the sections, on the other hand, the book reaches a high level. This is especially the case where the author describes diseases of which he has made a special study, such as syphilis of the brain, torular infections and intoxications. The extent of the subject is shown by the large textbooks on it which have recently appeared in Germany, and in a book of moderate size, of which a large part is devoted to illustrations, certain sections have to be reduced to the minimum. The book appears to be of chief value to those who are embarking on a study of the histology of the nervous system. They will certainly find in it clear descriptions of the cytological changes which are seen in the commoner nervous diseases.

*Volume jubilaire en l'honneur du Professeur G. Marinesco.* Pp. 715. Bucarest: E. Marvan. 1933.

The length and diffuseness of most medical writings is a source of well justified complaint by the student and busy practitioner who tries to keep up to date in his subject, and probably no specialist suffers more in this respect than the neurologist. Week after week journals and monographs present to him papers of inordinate length, and yet there are few of them from which the intelligent reader cannot summarize what is new or important on a post card. This volume, published by his friends to celebrate the seventieth birthday of the distinguished Roumanian neurologist, Professor Marinesco, contains sixty-seven separate articles and numerous illustrations in little over 700 pages. There is scarcely an uninteresting contribution among them, and many contain original observations of value or present older subjects from new points of view. Few of the writers seem to have suffered from the conciseness necessarily imposed on them, and the volume is as a whole therefore less tedious and more readable than such collections of separate articles usually are. Its writers represent almost every country in which neurology is practised as a speciality, and it is consequently a valuable mirror of present-day tendencies.

*An Introduction to the Study of the Nervous System.* By E. E. HEWER and G. M. SANDES. Pp. 147. London: W. Heinemann. 1933. Second edition. Price 21s.

The second edition of this book, which originally appeared four years ago, is considerably enlarged by the inclusion of new matter, but there is otherwise little change. It contains a large number of diagrams, some admirably simple, others unnecessarily complicated, and it has been the aim of the authors to present, with the help of these diagrams, as concisely as possible—and they frequently adopt tabular form—those elements of the anatomy and physiology of the nervous system which they consider necessary for clinical practice or for the purpose of examinations. In the latter object they may have succeeded, but it is doubtful if students of elementary medicine or those with a special interest in neurology will find this the easiest and most pleasing way to obtain some acquaintance with the structure and functions of the nervous system. The desire to omit nothing has made many of the anatomical chapters too elaborate and complicated, and owing to the method adopted the presentation of the subject is too diagrammatic and disconnected. In some instances the space might have been more usefully utilized ; for instance, three whole pages are occupied with diagrams of the connections of the small ganglia which lie in the fifth and seventh nerves, but the structure of the cerebral cortex is not illustrated. The physiology of the nervous system lends itself more readily to treatment on these lines and some of the chapters, as those on the reflexes and on the autonomic system, will be useful to students who can assimilate knowledge in this concentrated form.

*Multiple Sklerose und Erbanlage.* von F. CURTIUS. S. 215. Leipzig: G. Thieme. 1933. Price 18 M.

This book is the result of an extensive research undertaken on the lines of modern genetic investigation into the occurrence of anomalies or disease of the nervous system among the relations of patients suffering with disseminated sclerosis. The author's own experience and the facts which he has collected from the literature of the disease indicate that the occurrence of disseminated sclerosis in two or more members of a family is less uncommon that it is generally assumed to be, but his chief thesis is that, regardless of the etiology of the disease, there are many factors which may determine its onset, the form it takes or the course it runs, and the inherited constitution of the subject is one of the most important of these. His statistical inquiries show that affections of the nervous system are more common and more severe in the relatives of those afflicted with disseminated sclerosis than in the average population, and the influence of a neuropathic constitution must therefore be considered in any discussion on its etiology or pathogenesis.

*Les arachnoïdites spinales adhésives.* Par DEM. PAULIAN et D. TURNESCO. Pp. 95. Paris: Masson et Cie. 1933. Price 24 fr.

The condition with which English neurologists have been familiar under the titles "Circumscribed Serous Meningitis," or "Chronic Cystic Meningitis" for the past thirty years has lately attracted much attention on the Continent, and especially in France. As its pathology is still uncertain and its symptomatology indefinite and often confused, a monograph in which our present knowledge was critically reviewed and adequate facts collected to throw some light on its essential nature would be welcome. This volume scarcely satisfies these demands: the section on the ætiology of the disease is vague and nothing is added to the little we know of its morbid anatomy. The symptoms, which vary so much from case to case, are however carefully described and a series of plates illustrates the appearances most commonly found on the injection of lipiodol. The discussion of the indications for operation is also useful.

*Behaviour Mechanism in Monkeys.* By HEINRICH KLUVER. Chicago: University of Chicago Press. 1933. Pp. 387. Price 22s.

Dr. Kluver has carried out on monkeys an investigation so thorough and so critical that it may serve as a model for further research of the kind. It was done from 1926 onwards under the Behaviour Research Fund at the Institute for Juvenile Research, Chicago, and was intended to be a phenomenological study of animal behaviour. Such a biological approach to psychology is not new, but the author has extended it by the use of fresh methods and has tried to "correlate psychological mechanisms with brain mechanisms." This has not led, however, to any casual use of analogy as evidence of identity: throughout the book restraint and cautious examination of the evidence are conspicuous. The earlier part of the work is concerned with the general problem of behaviour mechanisms, and with methods and procedure; the last chapter is devoted to a discussion of the results in the light of various psychological theories and problems. Hypotheses for future work are put forward and their bearing on human psychology indicated. The author's grasp of the relevant literature is remarkable.

*Comment diagnostiquer, comment traiter, les maladies mentales.* Par L. NEUBERGER. Paris: Maloine. 1932. Pp. 424. Price 40fr.

This work is complementary to an earlier one by the same author on the treatment of nervous diseases. It is intended chiefly for the general practitioner, and its arrangement is very like that of the familiar handbooks in which easy means of reference and concise statement are preferred to detail and leisurely exposition. From this point of view it is admirable, but along with the customary French lucidity and precision there is the customary French lack of an index. The psychiatrist will be dissatisfied with the tabulated helps to differential diagnosis, so much more definite than the facts warrant, but he will be attracted by the insistence on constitution as the basis of the endogenous disorders, the unitary psychopathology offered for the affective psychoses, and the general sobriety of the author's approach. There is an unusual final discussion of the psychiatric fashions of the moment, which in France are mainly physiological and dualist.

*Psychoanalysis and its Derivatives.* By H. CRICHTON-MILLER. London: Thornton Butterworth. 1933. Pp. 256. Price 2s. 6d.

Psychoanalysis is nowadays a topic with which educated people are more or less familiar; many popular accounts, written with authority and lucidity, are available. Another book on the subject for the intelligent layman is only to be welcomed if it is more critical, more profound, or more comprehensive. It cannot be said that Dr. Crichton-Miller's book meets the first two of these requirements. It is comprehensive in that it has chapters on the doctrines of Freud, Jung and Adler, as well as the crepuscular Prinzhorn, but the psychoanalysis here presented is of a pleasing but unreal simplicity, and the criticisms are banal rather than penetrating.

The book may be regarded as a competent, though superficial, attempt to give the average man and woman a brief outline of some intricate, unfinished and all-embracing psychological theories of varying value and having little more than a historical connection with one another. This is undoubtedly a difficult task, but the author has succeeded in concealing the subtleties of the problem, and by a generous use of quotation has avoided personal colouring of the exposition. He passes over the difficulties and obscurities which vex analysts themselves, and by his disarming use of dilution and analogy, gives the reader the impression that there is very little to quarrel with in the views of any of these schools. In his last chapter he shows a confident, if vague, optimism, which foresees the sure discovery and conjunction of the valuable elements in all the warring theories. In psychoanalysis and its derivatives the good time coming seems so distant a millennium that aspirations towards it are epistemologically vicious for the psychologist, however useful the eclectic attitude may be for the psychotherapist.

*Stoke Park Monographs on Mental Deficiency and other Problems of the Human Brain and Mind.* No. 1. The Burden Memorial Volume. Edited by J. A. BERRY. London: Macmillan. 1933. Pp. 249. Price 10s. 6d.

It is difficult to understand for whom this book is intended; much of it is written in the style of a popular lecture, and if this were its purpose one might condone its carelessness as to fact and precise expression, its dogmatism, looseness of reasoning, tedious reiteration, and neglect of rules of scientific presentation.

The volume is explicitly called a monograph, but it is made up of contributions, representing "original research, study and thought," and "contributions to mental science." The customary scientific standards should therefore be applicable.

The main thesis of the book is the alleged structural changes in mental deficiency in the cerebral cortex, though no adequate histological evidence of this is furnished, and its relation to crude cranial capacity. Dr. Berry develops these points with much repetition of elementary anatomy, expression of personal convictions, and a vigorous use of the paralogism; his papers and those of which he is part-author constitute more than two-thirds of the present volume. Some of the contributions are trivial, as photographs of defectives; others are clinical reports with didactic or diagnostic commentaries. Otherwise the most interesting features of the book are the reports of the clinical findings in 162 adult feeble-minded women, and some psychologically ambitious but uncritical tests. There is a curious bibliography which, like the text, suggests the scrappiness of the contributors' equipment for dealing with problems that are neither simple, nor new, nor universally neglected.

*Fluctuations in Human Output.* By S. J. F. PHILPOTT. Cambridge: University Press. 1932. Pp. 125. Price 12s. 6d.

This paper appears to have more to do with mathematics than with psychology. The main purpose of the study was to discover whether curves of output, obtained from uninterrupted mental work, are essentially periodic, the waves being geometric in nature, i.e., of constant periods when plotted against the log of time. The findings indicated that this was so and also that there was a unit of logarithmic wave-lengths that seemed to be the same for all the subjects under all the conditions of experiments met with. There is nothing in the paper but its conclusions likely to be of interest to the medical reader.

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EDITOR.